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INTRODUCTION

MEDICINE as a science, an art and a communal effort belongs to the whole humanity.

The results of scientific research in human health and disease give *the medical science* its position in the academic world.

The skilful application of this knowledge to promote the health and combat the disease of fellow-beings is *the medical art* of every member of the Hippocratic profession the world over.

The human endeavour to let all members of every community have equal access to *medical care* is shown by all nations of the world.

The academic, professional and social activities in these spheres constitute the MEDICAL WORLD.

DANISH MEDICINE is a part of this world-wide medical life.

Being one of the many smaller countries of the world, *Denmark* is strongly aware of the great importance of the mutual give-and-take in all international co-operation. And speaking one of the languages which less than one per cent of all people can understand, we Danes realize the linguistic barriers in this global exchange of experience and ideas.

As an attempt to lessen this difficulty for the majority of the readers in the medical world we introduce the DANISH MEDICAL BULLETIN.

THE MEDICAL ASSOCIATION, the Medical Schools of our Universities and the Danish National Health Service — co-operating in this as in many other objects — are the sponsors of the new journal.

The Bulletin is at publication of the Danish Medical Association, and is supported by the Government through the Universities of Copenhagen and Aarhus and the National Health Service.

Once a month the Bulletin will accompany the weekly paper *Ugeskrift for Læger* to all members of the association and all subscribers of this periodical — its subscription fee not being raised.

In addition, the Bulletin will be *distributed* all over the world to medical schools, university libraries, teaching hospitals, scientific institutions, medical boards, the national medical associations etc. It is anticipated that these institutions in return will place the Bulletin on the mailing-list of their own publications.

A *personal subscription* for the Bulletin can be obtained through every book-seller the world over (see front cover).

INDEX MEDICUS DANICUS, hitherto published by the *University Library of Copenhagen* as a separate publication, in the future will be incorporated in the Bulletin, two of its monthly issues being devoted entirely to the Index so that this may be bound separately.

The other issues of the Bulletin are planned to bring yearly approximately 350 pages, giving *a survey of Danish Medicine today* in the form of original articles, short communications, annotations etc.

THE EDITORIAL BOARD consists of the editors of Ugeskrift for Læger, a representative of the Medical Faculty, University of Copenhagen, a representative of the Medical Faculty, University of Aarhus, and a representative of the National Health Service (State Medical Board).

The editors aim at a journal in which the Medical World may find a reflexion of all scientific, professional and social activities of Danish Medicine, presented in a condensed and yet comprehensive way.

It is hoped that this periodical will be accepted as it is aimed — to pay a small tribute to the World Medical Literature, reciprocating what Danish Medicine owes to it.

The Editors

MEASLES IN VIRGIN SOIL GREENLAND 1951

By POVL ELO CHRISTENSEN, HENNING SCHMIDT, H. O. BANG, VERA ANDERSEN, BJARNE JORDAL and OSKAR JENSEN

The consequences of epidemic outbreaks of measles in populations never previously exposed to the disease, or possibly exposed only in previous generations, have frequently proved catastrophic (1, 2, 6, 7, 10, 11). Until April 1951, the population of Greenland (approximately 22.000 individuals) had, to our knowledge, escaped this disease, a fact which is mainly attributable to the previous slower communications between Greenland and the surrounding world; this condition caused the outbreak of possible cases of measles to occur prior to the arrival in Greenland. Is was therefore possible to prevent the introduction of the disease by effective quarantine measures.

At the end of April 1951, the disease was, however, transferred from Copenhagen to Julianehåb by a Greenlandish seaman named Manasse, who prior to his departure from Copenhagen had been in contact with a compatriot, residing in that city who developed measles a few days later. In Manasse's case, the incubation period was extraordinarily long according to available information, viz. 19 days from the date of exposure until the appearance of the eruption and thus considerably exceeding the duration of the passage. On arrival in Julianehåb, Manasse was paid off and there he indulged in lively conviviality while still in the incubation period. Thus a few days prior to the appearance of the eruption (and probably while he had pronounced prodromal symptoms), he took part in an entertainment, typical for Greenland, a so-called »dancing-mik«, in which several hundred individuals were gathered in rather limited premises. These ideal possibilities for infection resulted in an epidemic, developing explosively and with simultaneous outbreaks in the town of Julianehåb and in several quite large settlements, whither the infection had been conveyed by individuals returning to their houses immediately after contact with the source of infection. From these foci, the epidemic spread and finally involved virtually all inhabitants of the District of Julianehåb (approximately 4,000 individuals). Thanks to the geographical features in combination with strict quarantine measures, the epidemic did not spread beyond this, the most Southern district of Greenland. It appeared, however, impossible to carry through effective quarantine measures in the separate settlements on account of the inability of the population to grasp the nature of the spread of the infection and the Greenlanders' gregarious nature.

A few words are necessary on housing conditions in Greenland in order to explain how the morbidity of an epidemic of measles in an area of such vast extent attained nearly 100 per cent. (vide infra) in less than 3 months. The houses are very small and, as a rule, consist of one room only. Each house accomodates, on an average, 6 individuals but isolated houses are encountered where 12 to 15 human beings live in a single room, providing approximately one m^2 floor space per occupant. The principal furniture is a wooden plint where all the occupants sleep close together. Obviously, the possibilities for spread of the disease are maximal.

In order to counteract the serious effects which an epidemic of measles under such conditions might be anticipated to cause, assistance was immediately sent from Denmark by air to the region affected, because the public health personnel could not be expected to cope with the situation unaided. In addition to drugs, 13 nurses and 5 physicians were sent. In this way it was possible to put into action a treatment which was relatively effective when it is considered that all treatment had to be undertaken in the patients' homes as all beds in the two hospitals were already occupied by patients with tuberculosis. Simultaneously, a quite detailed registration of the course of the epidemic as well as a great part of the case-histories were successfully obtained. Out of the native population of the District, 4,320 cases were registered (i. e. nearly all) and out of these, a total of 2,164 patients were followed by daily examinations. Nearly all accounts of the disease are therefore based upon information about these patients. The account of the mortality and the description of the course of the epidemic are based upon the entire material.

Of the 2,164 patients, already mentioned, who were carefully examined, 507 were treated prophylactically with convalescent serum or gamma globulin (vide infra).

COURSE OF EPIDEMIC

In Table 1, a survey is given of the native population in the District attacked by the disease. It appears from this that 31 Greenlanders had had measles previously (during sojourns in Denmark). None of them became re-infected despite intense exposure. 32 who had not previously had the disease avoided infection. Out of these 32, however, 27 had received specific treatment with antisera, i. e. only 5 individuals who were not treated prophylactically out of a total of 4,262 susceptible individuals did not contract the disease, corresponding to a morbidity of 999 ‰. Two of these five Greenlanders were probably not exposed to infection as they lived in an isolated

From Statens Seruminstitut, Copenhagen (Director: *J. Ørskov*, M. D.), Grønlandsdepartementet, Copenhagen (Medical Advisers: *T. Thune Andersen*, M. D. and *Sylv. M. Saxtorph*, M. D.), Blegdamshospitalet, Copenhagen (Professor *H. C. A. Lassen*, M. D.). The present paper is an extract from several communications previously published in Acta Med. Scand.

Table 1.
All Registered Persons in the Julianehåb District.

Age	Sex	No. of inhabitants	No. of measles cases			Probably measles no rash	No. of persons without measles			Measles previously
			+ proph.	− proph.	Total		+ proph.	− proph.	Total	
<1 year	♂	93	72	13	85	2	6	0	6	0
	♀	108	89	12	101	0	7	0	7	0
1 year	♂	64	51	11	62	0	2	0	2	0
	♀	73	49	22	71	0	2	0	2	0
2—14 years	♂	731	116	608	724	0	4	2	6	1
	♀	732	149	580	729	2	0	0	0	1
15—34 years	♂	656	92	556	648	1	1	0	1	6
	♀	734	135	587	722	2	1	0	1	9
35—54 years	♂	322	44	275	319	2	0	1	1	0
	♀	465	78	376	454	4	1	2	3	4
>55 years	♂	134	36	80	116	10	3	0	3	5
	♀	198	49	132	181	12	0	0	0	5
No information ...	♂	3		3	3					
	♀	7		6	6	1				
Total	♂	2,003	411	1,546	1,957	15	16	3	19	12
	♀	2,317	519	1,715	2,264	21	11	2	13	19
	♂+♀	4,320	960	3,261	4,221	36	27	5	32	31
Per cent of total population:			22.2	75.4	97.6	0.8	0.6	0.11	0.7	0.7

house in which the other occupants had had the disease some weeks previously during a sojourn elsewhere.

Thirty-six individuals must be regarded as having had measles although no eruption was observed; the majority of these cases (i. e. 24 out of 36) developed a pyrexial condition at a period when infection was probable and died before the eruption appeared. This happened mostly in elderly feeble individuals or tuberculous patients in an advanced stage. Among the 12 patients who survived in this group, a few very old individuals (over 80 years) were found in whom the dark pigmented mottled skin was perhaps the cause why eruption was not observed. These few cases may perhaps be interpreted as abortive; apart from this, no spontaneous abortive course of the disease was seen. Of the 36 patients mentioned, 9 received specific prophylactic treatment which perhaps was the reason why the eruption did not appear.

The length of the incubation period is generally stated as being quite constant (13—14 days); this was particularly observed by P a n u m during the Faroe Islands epidemic in 1846. Judging from the first wave of the epidemic in Greenland it was found that the majority of the infected population conformed to an incubation period of this duration. Quite a few, however, showed a shorter incubation period; in a number of cases it was 7—9 days and in some cases as short as 4—5 days, *calculated from the appearance of the exanthema in the preceding case.* Incubation periods of more than 13—14 days cannot be deduced from the curve of the epidemic because many individuals were exposed to infection more than once. That the incubation period, however, may be longer than 14 days appears from the case of Manasse.

Epidemic curves were prepared for all settlements. Despite isolated minor differences, attributable to the varying possibilities of contact with the first sources of infection, all curves had, by and large, the same configuration, demonstrating two peaks, the second peak representing the maximum. The interval between the two peaks was ten days on all the curves. Following these two peaks the epidemic nearly subsided after having involved nearly all the inhabitant. Only extremely few cases occurred more than 40 days after the first case in a locality.

It is striking that this epidemic in scarcely 3 months attained a morbidity of nearly 100 per cent. Since the epidemic in this extensive area spread so rapidly, this must be ascribed to the gregarious nature of the Greenlanders which implied that they were inclined to visit their neighbours even when ill, in addition to the housing conditions mentioned already. The contacts in the shops, upon the supplies of which the Greenlanders are very dependent, also played a great part.

COURSE OF THE DISEASE

The course of the disease *in 1,657 patients not treated prophylactically* is described in detail in the original articles. It presented no principal differences from the picture of the disease generally known, for which reason only isolated facts of interest will be pointed out here.

The prodromal stage varied from 0—8 days but was in two thirds of the patients (66.7 per cent.) 2—4 days. Surprisingly enough, conjunctivitis was only slight. At this stage, a very distinct enanthema occurred in the majority of patients; it was, as a rule, markedly haemorrhagic and extending over the hard and soft palates and the mucosa of the cheeks. This pronounced haemorrhagic enanthema, only rarely seen in Denmark, is perhaps connected with the well known tendency to haemorrhage found in Greenlanders. In 266 patients, in whom the oral cavity was inspected daily, enanthema was found in 75 per cent. and Koplik's spots in 50 per cent. Epistaxis occurred frequently in the initial stage.

The exanthema did not differ from the ordinary type. It was haemorrhagic in a couple af cases only.

Complications. The nature of these did not differ particularly from those ordinarily known, whereas the frequency, as apprehended, greatly exceeded that described under other conditions. Complications developed thus in 45.7 per cent. of the cases, viz. 39.9 per cent. of males and 51.3 per cent. of females. *Pulmonary complications* in the form of capillary bronchitis and bronchopneumonia comprised 81 per cent. of all complications, and 35 per cent. of males and 45 per cent. of females had symptoms of pulmonary affection. It should be stressed that pneumonia developed very early: in 50 per cent. of the cases in immediate connection with the appearance of the exanthema or even in the prodromal stage. The authors formed the impression that contagious factors were also active as regards pneumonia as in certain houses with particularly poor hygiene, where particularly many individuals were ill simultaneously, many and serious pneumonias were encountered. A numerical calculation on a larger number of patients did not, however, reveal any definite correlation between the frequency of complications and the number of inhabitants per house.

Otitis media constituted 9.7 per cent. of all complications. In the majority of cases, it developed 3—4 days after the appearance of the exanthema, disappeared rapidly during treatment with penicillin and did not necessitate myringotomy in any case. The relatively infrequent occurrence of this complication, so common elsewhere, may be explained by the fact that cases with pneumonia, a complication which developed early in the course of the disease, were treated immediately with penicillin.

Cardio-vascular insufficiency in the form of pulmonary oedema was presumably the most serious complication in this epidemic although the incidence was not great. Among the 1,657 meticulously registered patients, not treated prophylactically, 18 cases were encountered, i. e. 2.2 per cent. of the total number of complications. With one exception, the cases of pulmonary oedema occurred in patients over 35 years of age (of whom 10 were over 55 years of age). Out of these 18 cases, 13 occurred in females of whom 4 were pregnant or puerperal. Treatment with morphium, euphyllin-glucose and venesection proved life-saving in isolated cases but, on the whole, the prognosis was poor. Stærmose & Kofoed (12) described 3 similar cases which occurred during an epidemic of measles on the Faroe Islands in 1938 and which took a fatal course. Yet as a rule, this seems to be a complication which is not seen in areas where measles appear endemically, probably because the disease in those areas primarily affects children.

Encephalitis was encountered in 6 out of the 1,657 patients and offered no opportunity for particular observations. *Adenitis* described in the literature as a common complication, was observed in 4 patients only and was not suppurative in any of these. *Eye diseases* were not encountered during the epidemic proper but in the succeeding months, several patients consulted the physicians for phlyctenular processes.

The maximal temperatures and the number of days with pyrexia deviated only little from the conditions in patients without complications. This the authors are apt to ascribe to the rapid and, in the majority of cases, effective *treatment* of complications which consisted of daily injections of 300,000—400,000 units of penicillin. Oral treatment with sulphonamides was employed in isolated cases only, as the oral mode of administration was not suitable under the special conditions in Greenland.

MEASLES AND PREGNANCY

During the epidemic, 83 women were registered as pregnant or puerperal; the majority of the pregnant women were in the second half of pregnancy. It should be pointed out, that in Greenland abortion is an extremely rare occurrence under normal conditions. All the pregnant women got measles; in 7, however, the disease occurred during the puerperium. Among the remaining 76 pregnant women, delivery or abortion took place in 26 during the course of the disease. In 13 cases out of the 26, delivery occurred at term while in 6 cases delivery was premature and 7 abortions in the 3rd—5th months were encountered. Of the infants born at term, 3 died within the first 24 hours and of the 6 premature infants, 3 died. No case of congenital measles was observed, and no congenital malformations were observed in children, the mothers of whom suffered from measles during the pregnancies concerned.

No preponderance in the incidence of pneumonia in pregnant women could be demonstrated

with certainty but pregnant or puerperal women showed predisposition to pulmonary oedema which occurred in 7 patients in this category. One of these patients died on the third day post partum. With this exception, the prognosis proved relatively favourable in these cases, provided that the therapy previously described was instituted in due time.

The issue was fatal in 4 out of the total number of pregnant or puerperal patients.

MEASLES AND TUBERCULOSIS

Tuberculosis is a common affliction among the natives of Greenland. The result of various investigations shows a morbidity varying between 10 and 20 per cent. (5). There were reasons to anticipate that the epidemic of measles might prove detrimental to the tuberculosis situation because previously latent tuberculosis might become activated, and because measles in patients with active tuberculosis and in poor condition would be liable to end fatally.

As it happened, the majority of the inhabitants of one of the larger settlements (Narssak) had been subjected to examination for tuberculosis about a month prior to the outbreak of the epidemic; the examination comprised X-ray screening and, in a number of cases, examination of sputum. On renewed examination about 3 months after the cessation of the epidemic, the following facts were stated: *of the total number of individuals examined* 352 appeared at both examinations*); on the second examination, all the cases of pulmonary tuberculosis,, diagnosed on the first examination, were re-encountered but, in addition, 19 individuals were encountered in whom screening had not revealed any abnormality on the first examination but showed infiltrative lesions on the second examination; and in 13 of these patients, tubercle bacilli were demonstrated in the sputum. Further, remnants from pleurisy not previously observed were revealed in 8 patients. These findings appear to show that the resistance to tuberculosis is lowered by measles.

In one settlement, an investigation was carried out concerning the behaviour of the tuberculin reaction during infection with measles. Moro's reaction was employed in 51 patients at regular intervals of 3—4 days, commencing at the appearance of the exanthema, at which stage the reaction was negative, and repeated until a positive reaction appeared. In the majority of cases, the reaction became positive again 8—12 days after the appearance of the exanthema but in isolated cases, the reaction did not become positive again until after 30—35 days. In this connection it may be mentioned that post-primary erythema nodosum was observed in isolated cases after sustained measles. A total of 9 such cases are registered in the authors' material but this figure is probably minimal as the phenomenon in some cases was observed 1—2 months later, i. e. at a time when, as a rule, physicians and nurses had left the locality. The etiology of these cases is interpreted as tuberculous, probable the expression of a conversion of the organism after tuberculous allergy had been temporarily abolished by measles.

*) In addition to these individuals, 15 were examined at the first examination who died during the epidemic or during the following 2—3 months. Of these, 9 showed pulmonary tuberculous changes and in 7, tubercle bacilli were demonstrated.

SPECIFIC SERUM PROPHYLAXIS*)

With the object of attenuating the disease in the weakest individuals, prophylactic treatment with either convalescent serum or gamma globulin was employed to a great extent. An analysis was made of the effect of this treatment in 520 individuals, of whom 50 were treated with convalescent serum and the remainder with gamma globulin. No difference was found between these two groups.

Prophylactic treatment was administered to children under 2 years, pregnant women, tuberculous patients and patients weakened by other causes and in this category individuals over 60 years were included as far as supplies allowed.

The dosage for children under 15 years was, by and large, the same as is usually stated as providing a pronounced degree of protection when administered in due time. On the other hand, the adults received a dosage which was too small for optimal protection to be anticipated.

Of 520 individuals treated prophylactically, 97.5 per cent. developed measles, a significant deviation from the morbidity (99.8 per cent.) in the untreated patients. The prophylactic treatment evidenced itself distinctly in an attenuated picture of the disease, characterized by a shortened prodromal stage, paler exanthema and fewer pyrexial days.

The prodromal stage was thus considerably shortened in the patients treated prophylactically, in so far as nearly 40 per cent. had prodromal symptoms for 0—1 days only. The enanthema and Koplik's spots occurred as frequently in the patients treated prophylactically as in the untreated cases.

The exanthema was, as a rule, less pronounced in the patients treated prophylactically. It was frequently confined to the head and neck only and often appeared in the form of small macules with much less confluence than in the normal well developed exanthema of measles.

The difference between the maximum temperatures in patients treated prophylactically and those not treated prophylactically was not particularly pronounced, a fact which also has been

*) As regards the complicated conditions in »Specific serum prophylaxis«, those particularly interested are referred to the article by Elo Christensen and Henning Schmidt in Acta Med. Scand.

observed by others (4). On the other hand, there was a distinct difference in the number of pyrexial days (in patients without complications), as 50 per cent. of the patients treated prophylactically had fewer than 5 pyrexial days and only 5 per cent. had more than 8 pyrexial days. Among the patients not treated prophylactically and without complications, only 26 per cent. had less than 5 pyrexial days while 11 per cent. were pyrexial for more than 8 days.

The nature of the complications was the same as in the patients not treated prophylactically; 82 per cent. were pneumonias, 11 per cent. otitis media while 7 cases of cardiac insufficiency in pregnant women or elderly patients occurred. On the other hand, the total frequency of complications in the patients treated prophylactically (28.4 per cent.) was significantly lower than for patients not treated prophylactically (45.7 per cent.). These conditions held true for the individual age groups under 55 years. Over this age, the difference was not so distinct.

Since the effect of prophylactic treatment is less pronounced than usually, this probably is due to the exceptionally heavy exposure during the epidemic often continuing for weeks. This has been explained by others (8, 9) as being due to large infecting doses of virus together with repeated exposure within a limited period at time, resulting in greater frequency of the disease.

MORTALITY

The total mortality among *all 4.257 patients with measles in the district* was 18 per thousand (16 ‰ for males and 20 ‰ for females).

Among *the 3.273 patients not treated prophylactically*, the mortality was 15 ‰ (12 ‰ for males and 17 ‰ for females). Several deaths occurred in the prodromal stage (25 out of 77) and the majority of the remainder within 14 days after the occurrence of the exanthema.

The mortality was greatest in the age groups over 55 years (159 ‰ for males and 104 ‰ for females), second largest in children under 1 year (46 ‰ for boys and 10 ‰ for girls) and least in the group between 2 and 14 year (0). The cause of death was cardiac insufficiency in one third of the cases, tuberculosis in one fifth and pneumonia in one sixth. Four patients died with symptoms of encephalitis.

The mortality among *507 patients treated prophylactically* was 34 ‰, a figure which naturally cannot be compared directly with the foregoing figure as this group contained all the »poor risks«. If the patients who died from tuberculosis together with newborn infants be excluded from both these groups of patients, the mortality for patients treated prophylactically (6 ‰) is only half that for patients not treated prophylactically (12 ‰). The tuberculous patients who died in connection with measles were all in such an advanced stage of tuberculosis that the occurrence of death was only slightly premature.

SUMMARY

A report is given of an epidemic of measles in virgin soil (South Greenland).

The morbidity rate attained 99.9 %. Of the 4257 patients with measles, 45 % developed complications, pneumonia being the most frequent. Several cases of heart failure (pulmonary oedema) were encountered. In several pregnant patients, abortion or premature delivery occurred.

No case of congenital measles was observed.

No congenital abnormalities were observed in children, whose mothers suffered from measles during pregnancy.

The total died rate amounted to 18 per thousand.

Investigations on the morbidity from tuberculosis in 352 individuals before and after the epidemic of measles indicate that measles may cause aggravation of the tuberculosis. The temporary reduction or absence of tuberculous allergy during infection with measles was confirmed.

Several cases of post-primary erythema nodosum were observed.

Prophylactic treatment with convalescent serum or gamma globulin during the epidemic had only a slight effect in reducing morbidity.

To a great extent, attenuation of the disease was obtained. This was manifest in reduction of the prodromal symptoms, diminished intensity of the rash and fewer days of pyrexia.

The frequency of complications in patients under the age of 55 years, treated prophylactically, was significantly lower than in patients of the same age groups not treated.

The death rate was lower among the patients treated prophylactically, when deaths among tuberculous patients and premature infants were excluded. Death from tuberculosis occurred among patients where the disease was at a hopeless stage. No definite statement can be made here concerning the effects of measles prophylaxis in tuberculous patients, because no control material is available.

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POLIOMYELITIS IN COPENHAGEN 1952

By H. C. A. LASSEN

The metropolitan area of Copenhagen has a population of about 1,200,000 inhabitants served by one hospital for communicable diseases, the Blegdam Hospital, with about 500 beds. During the last 5 months of 1952 we received about 3,000 patients with the diagnosis of poliomyelitis, roughly one third with paralysis and two thirds without. This, of course, was quite extraordinary, but still more extraordinary was the high incidence of respiratory insufficiency with or without impairment of swallowing. Almost one third of the paralyzed patients belonged to this group.

At times we had seventy patients requiring artificial respiration; around New Year fifty to sixty patients still required artificial respiration. Today between 25 and 30 remain from the 1952 epidemic still dependent on artificial respiration.

The epidemic culminated about the 1st of September. During the week of August 28th to September 3rd our hospital admitted 335 patients with polio, or nearly 50 cases daily. About one tenth of these patients were suffocating or drowning in their own secretions.

We felt as in a state of war, ill equipped, both theoretically and practically, to cope with a catastrophe of such magnitude. We had one tank respirator (Emerson) and six cuirass respirators at our disposal. This equipment naturally proved wholly inadequate when the epidemic got into its stride.

We had to improvise, we had to find ways of avoiding the impossible situation of having to choose which patients to treat in the available respirators and which patients not to treat. Every patient should have an equal chance of survival.

In former years our therapeutic results in cases with respiratory insufficiency and involvement of the lower cranial nerves and the bulbar centres had always been very poor.

During the eleven years 1934—1944, respirator treatment was used in 76 cases with a mean mortality rate of 80 per cent. Only cuirass respirators were used.

Thus, the prognosis of poliomyelitis with respiratory insufficency was rather gloomy at the outbreak of the 1952 epidemic in Copenhagen.

In the beginning of August, when it became evident that an epidemic was imminent, one of my assistants, Dr. L i n d a h l, with the assistance of 6 senior medical students, was put on the job of visiting all the homes of the polio patients. We drew up an extensive questionnaire including a host of questions. After eliminating all the questionable cases of polio, about 2,300 cases of poliomyelitis remained — paralytic or non-paralytic.

All the non-paralytic cases had clinical meningitis and pleocytosis.

Paper read before The Royal Medico-Chirurgical Society of Glasgow, Oct. 23rd, 1953.

Our polio material and a carefully selected control material were compared in many respects. They were exactly identical with respect to age, sex and district of town. Only in one single respect a highly statistically significant difference was found, viz. concerning contagiousness. About 60 per cent. of the patients in the poliomyelitis material had been in contact either with patients with the diagnosis of polio, that is to say *our* diagnosis of polio, or with patients with minor illness, i. e. ephemeral febrile disease — as compared with 9 per cent. in the control group. And, naturally, the control group chosen at random included some few polio patients.

The figures are strongly suggestive of the person-to-person contagiousness of poliomyelitis.

During the first 3—4 weeks of the 1952 epidemic patients kept pouring in, many of them with respiratory insufficiency and impairment of deglutition. They nearly all died and our situation became increasingly desperate.

On August 25th we decided to call into consultation our anesthetist colleague, Dr. B j ø r n I b s e n, as we thought positive pressure breathing as used in modern anesthesia might be of value, and on August 27th the first patient received the treatment, which rapidly became our method of choice in patients with impairment of swallowing and reduced ventilation — viz., tracheotomy just below the larynx with insertion of a rubber cuff-tube into the trachea, and manual positive pressure ventilation from a rubber bag (bag-ventilation).

We were now in a position to treat every single patient requiring respiratory aid. In this manner we avoided being placed in the predicament of having to choose.

During the following weeks, 30—50 patients daily were admitted, including 6 to 12 per day with deficient respiration and (or) insufficiency of swallowing. All these patiens required special treatment.

At the height of the epidemic the staff of doctors permanently on the job was 35 to 40; we had about 600 trained nurses, and 250 medical students coming in daily and working in relays.

Fig. 1 shows schematically the various parts of the simple equipment used by us in about 200 patients subjected to manual bag-ventilation. The

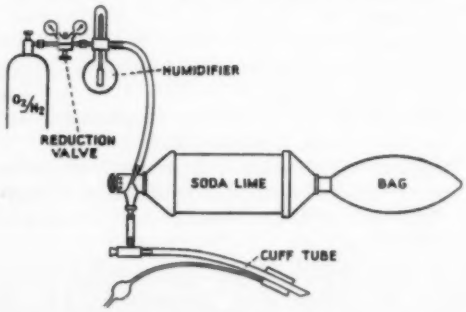

Fig. 1.

upper part af the cuff-tube has a side branch connected with a metal container packed with granulated soda lime (Waters's canister), from which a rubber tube goes to a cylinder containing equal parts of compressed oxygen and nitrogen. A rubber bag is attached to the one end of the canister, and a valve at the other end permits regulation of the pressure in the system. The cuff tube is closed with a rubber stopper. If aspiration is needed, the stopper is removed and a Tiemann's catheter is introduced mounted on a jet suction apparatus. The ejector effect of a cylinder containing compressed air, which is very effective and independent of electric power was most frequently employed. A good humidifier is essential, otherwise incrustation of secretions may occur.

In the acute stage several competing factors are involved, often difficult to diagnose and difficult to differentiate. These are: virus disease of the central nervous system, hypoxia, retention of carbon dioxide and vasomotor shock. In most cases one or more of these syndromes are present, the patients presenting a mixed clinical picture. Only careful clinical observation, supplemented by various biochemical tests can guide us through this jungle of diagnostic difficulties and lead to a rational therapy.

Our patients with respiratory insufficiency and (or) impairment of deglutition were treated in one or the other of the four following ways, frequently in combination:

1: tracheotomy and positive pressure ventilation,
2: tracheotomy alone,
3. respirator — tank or cuirass,
4: postural drainage and in-dwelling stomach tube.

The indications were:

1: for *tracheotomy and positive pressure ventilation:* accumulation of secretions in the upper air-ways,
insufficiency of swallowing,
ineffective cough and
a rapidly decreasing vital capacity;
2: for *tracheotomy alone* eventually in combination with in-dwelling stomach tube with continous suction and postural drainage:
pooling of secretions in the hypopharynx,
paralysis of swallowing,
ventilation normal of slightly to moderately decreased;
3: *respirator alone:*
respiratory insufficiency without accumulation of secretions;
4: *postural drainage,* often in combination with an in-dwelling stomach tube:
impairment of swallowing without stagnation of secretions or slight accumulation of secretions and normal or slightly deficient respiration.

I am quite aware of the fact, that we may be accused of having used tracheotomy and bag ventilation too freely. Yet, in 40 per cent. where tracheomoty and bag ventilation was the final therapeutic meassure, treatment had begun with postural drainage or in a respirator. In all these cases we had to resort to tracheomoty and bag ventilation as a more radical therapy because of alarming symptoms of suffocation.

After the introduction of bag ventilation on August 26, 321 patients requiring special therapy were treated according to the principles already mentioned. On 265 of these, i. e. 82 per cent., tracheotomy was performed and 232 of these had manual bag ventilation. The mean mortality rate fell from above 80 per cent. before August 26 to just under 40 per cent. for the whole group (date of reference: April 1st, 1953).

Of the 119 patients who died, 23 died during the first 24 hours after admission, while 77 died during the first seven days. This gives an impression af the severity of the epidemic.

Tabel 1.

Group	Period of admission	No. of cases	Died	Died within three days
I	July 24—Aug. 25	31	27 (87 %)	19 (70 %)
II	Aug. 26—Sept. 8	50	26 (52 %)	7 (27 %)
III	Sept. 8—Sept. 23	50	24 (48 %)	8 (33 %)
IV	Sept. 23—Oct. 5	50	19 (38 %)	10 (53 %)
V	Oct. 6—Oct. 21	50	13 (26 %)	7 (54 %)
VI	Oct. 21—Nov. 6	50	18 (36 %)	10 (55 %)
	Total II—VI....	250	100 (40 %)	42 (42 %)

Table 1 shows mortality rates in 281 patients requiring special treatment. Of the group treated during the first month of the epidemic before bag ventilation was introduced 87 per cent. died.

The next five groups, each comprise 50 consecutive cases in chronological order without any omissions. The table shows that the mortality rate for these patients, of whom the great majority was treated by tracheotomy and bag ventilation, was reduced from over 80 per cent. to about 40 per cent., representing about 100 lives. We are convinced that by far the greater part of these patients were saved by early tracheotomy combined with bag ventilation. Here also, the date of reference is April 1st.

The table also shows a continuous drop in mortality rate, from Group II to Group VI from 52 to 26 per cent. This probably is due to the fact it naturally took some time before the treatment, including adequate instruction of the hundreds of medical students employed (about 1,000 altogether) could be organized so that the bag ventilation was correctly administered. Observing the decreasing mortality rate during the course of the epidemic, we naturally searched for evidence of decreasing severity of the bulbar cases but could not find any, a clinical impression which is supported by the somewhat higher mortality rate in Group VI.

Since this survey was made only comparatively few patients have died; to date about 130 have died out of a total of 350 requiring special treatment. 150—160 patients have been discharged with varying degrees of peripheral paralysis, yet, quite a fair number with no or only slight residual paralysis.

60—65 patients are still in the hospital and of these about 25 are still dependent on artificial respiration. Only very few of these unfortunates will ever regain enough spontaneous respiration to get rid of respiratory aid. In nearly all these patients ventilation has been mechanized. Not one single patient is in a body respirator.

We do not think that this method is ideal. It certainly needs to be perfected. To some extent this has already been achieved, but we are still attempting to improve it.

However, in comparison with results formerly obtained in our hospital, it seems fair to regard the results as satisfactory under the circumstances.

CONCLUSIONS

In 1952 the Blegdam Hospital, Copenhagen, received 345 patients with life-threatening poliomyelitis of whom 333 had respiratory insufficiency.

As mechanical equipment was wholly inadequate, positive pressure ventilation was introduced.

The method consists in high tracheotomy with insertion of an inflatable rubber cuff-tube into the trachea and manual positive pressure ventilation from a rubber bag (bag-ventilation) in combination with repeated aspiration and bronchoscopy, postural drainage and stomach-tube.

Through this procedure mortality rates were reduced from over 80 per cent to under 40 per cent.

TREATMENT OF RESPIRATORY COMPLICATIONS IN POLIOMYELITIS

THE ANÆSTHETIST's VIEWPOINT

By BJØRN IBSEN

On the 25th of August 1952 I was called in as anæsthetist for consultation by Professor L a s s e n in the Blegdam Hospital of Copenhagen.

Within the preceding 3 weeks there had been 31 patients with bulbar poliomyelitis treated in respirators — tanks as well as cuirass. 27 had died. The number of patients coming in was still increasing, and all available respirators were in use. After having seen the condition of the patients in the respirators I felt, that as was impossible to evaluate in this complicated clinical picture, which symptoms were due to the disease and which due to inadequate ventilation.

4 patients were seen in the autopsy room that day. One of these — a 12 year old boy — had died in a respirator with a blood pressure of 160 and a bicarbonate level in the serum far above normal. The lungs did not appear to be sufficiently congested to make adequate ventilation impossible.

With enthusiastic encouragement from Professor L a s s e n I tried to demonstrate on a patient how sufficient ventilation could be administered without the help of a respirator.

A patient in a very bad condition was chosen for this. She was a 12 year old girl who had paralysis of all four extremities. She had atelectasis of the left lung and was lying on the side in Trendehlenburg position gasping for air and drowning in her own secretions. Her temperature was 40°2 C. She was cyanotic and sweating.

A tracheotomy was done immediately under local anesthesia, and a cuffed endotracheal tube put in place through the tracheotomy. During this procedure she became unconcious. A to-and-fro absorbtion system was connected directly to the tube. Good endotracheal suction was done. Even then it was impossible to inflate the lungs, partly due to secretions and partly due to bronchospasm. In this desperate situation I gave her 100 mg Pentothal i. v. in the hope that I could stop her struggling. She collapsed, her own respiration stopped and I found, that I could now inflate her lungs.

Shortly after this a device for continous measurement of the carbon-dioxide concentration in the air from one of the main bronchi — a Brinkman Carbovisor — and an Oximeter of the Millikan type, was put to work.

By these means it was shown, how underventilation gave rise to a CO_2 accumulation — even when full oxygenation of the blood was maintained with pure oxygen.

The usual signs of CO_2 retention could now be demonstrated. There was a rise in blood pressure. The skin became clammy and sweating — and the patient started her own respiration, which soon became gagging and bucking — a well known sign from some of the other patients seen in the respirators. Secretions began to pour out of the mouth and the nose.

These symptoms could be relieved within a few minutes, when CO_2 was removed by increasing the ventilation.

Another important point could be demonstrated on this patient. As soon as CO_2 was removed the blood pressure dropped to 80 — and the patient appeared to be in shock. Blood was given which improved her condition remarkably. The patient became warm dry and pink — which always makes an anæsthetist happy.

X-rays showed that the atelectatic left lung had been inflated completely.

So far, the patient had been improved by measures usually carried out by the anæsthetist during his daily work in the operating theatre: Active securing of free airway — adequate assisted ventilation, and intravenous treatment of shock.

Read at the Royal Society of Medicine, London, Oct. 16, 1953.

The patient was now put in a respirator. All the signs of underventilation occured, and she begame once again cyanotic. Administration of oxygen in the same way as to other patients in respirators revealed, that her colour could be improved- and nearly full oxygenation ensured — but the carbovisor showed a continous rise in CO_2.

When the respiration was assisted in the respirator by intermittent squeezing of a bag connected with the tracheotomy-tube, everything went well again. In this patient then we had to continue the manually assisted respiration, because it was impossible for the respirator to maintain sufficient ventilation to secure the necessary elimination of CO_2.

Why was this impossible?

The reason was thought to be, that the patient already had too many lung complications, which seemed to make the respirator inefficient in this case.

The aim should be to protect the lungs against secretions, before the patient is put into a respirator.

The experience from a couple of late emergency trachetomies, done under local anesthesia confirmed this.

The operation itself was difficult — performed on the bed or in a respirator. The patients were apprehensive and uncooperative probably due to anoxia. Bleeding into the lungs could not be avoided. During the handling of the trachea, anoxia was further aggravated due to spasm and reflexes. Finally some of the patients suffered from severe vomiting and aspiration.

These emergency tracheotomies done late in the disease are almost useless. I do not remember many patients who survived a late procedure more than a few days.

Accordingly it was felt necessary to have an endotracheal cuffed tube, which had been passed through the mouth, lying in the trachea before the tracheotomy should be performed.

A general anæsthesia therefore very often had to be administered before this could be done.

By this means, a free airway was maintained during the operation, and the respiration could be assisted as well, if needed. The surgeon had quiet operational conditions. The bleeding could be under control before the tracheotomy-tube was inserted through the tracheotomy-opening.

The first patient operated in this way, was found the next morning to have been seriously overventilated by the respirator during the night.

From then on the first approach to the treatment was outlined:

1. Any period of anoxia has to be avoided.
2. When necessary a tracheotomy should be performed, and a cuffed endotracheal tube inserted through the tracheotomy, in order to protect the lungs against secretions from above — allowing effective endotracheal suction — thus securing a free airway.
3. The tracheotomy should be preceded by oral intubation. Most often this had to be done under general anesthesia.
4. Assistance to inadequate ventilation could be given when necessary, by connecting the tracheotomy-tube with a to and fro absorber-system, and then manually performing an intermittent positive pressure ventilation. This could be done to patients in, as well as out of respirators.
5. Shock should be treated with intravenous infusions — blood and serum — or vasopressor drugs, after the same principles as in surgical shock.

As soon as we realized, that we actually could do something for the patients in the respirators, when these seemed to be insufficient, we were running around doing this resuscitation job — treating atelectasis — taking patients out of respirators, and ventilating them properly for half an hour, putting them back again. Treating shock and so on.

It was obvious, that the work of treating the respiratory emergencies just described, was so big, that it could not be done by the usual hospital staff. Naturally the help was looked for from anæsthetists, who were familiar with this type of treatment. Accordingly the anæsthetists of Copenhagen were mobilized.

In addition we were fortunate in having at this time established in Copenhagen a W. H. O. anesthesiology center, Some 20—30 trainees attending this center were available for help. Within 4 days the anæsthesia-help was organized. Every 4th day the anæsthesia-service from one of the four biggest Copenhagen hospitals took over.

Very soon so many patients had to be put on manually controlled ventilation, that medical students had to perform this work as well.

After 8 days a big organisation was working.

All patients with respiratory problems were collected in a special department, where they were under constant observation by a team, consisting of the epidemiologist, the ear-nose-and throat-man, the anæsthetist, all working with the help of an excellent and capable laboratory — which was staffed by two full-time specialists and 15 technicians. Later on X-ray people and physiotherapists joined in as well.

There were already in this department 3 floors, each with 35 patients, most of whom had their own room.

To give you an impression of the magnitude of the task, I can tell, that after these 8 days, we had 75 patients who needed constant artificial respiration by some means. There were within 24 hours, 260 extra nurse auxillaries, 250 medical students, 27 technicians to handle the 250 big cylinders of gases used. 12 new patients entered this special department that day.

In order to secure the continuity in the treatment, conferences were held every single day for 2 hours in Professor L a s s e n's office, where all

problems were discussed. Specialists were invited to attend these conferences, — physiologists, cardiologists, neurologists and so on.

It shows what a tremendous organisation Professor Lassen had to build up in a short time. I can only give you a fragment of the whole picture, as it looks from an anæsthetist's point of view.

Patients from the general wards — there were 500 beds, and 50 to 60 new cases coming in every day — were transferred to the special department mentioned, when they showed any of the following signs of respiratory impairment:

Difficulty in swallowing.

Accumulation of secretions in the airway.

A weak and insufficient cough — when the intercostal muscle or especially the diaphragm became paralytic.

Paresis of the upper extremities.

Progressive paresis moving upwards.

Marked »encephalitic« signs.

On the observation-ward a record similar to those kept by anæsthetists during operations, was started. Blood pressure — pulse — respiration was taken every ¼ hour. Temperature every full hour. Continuous laboratory investigations were carried out.

We tried to follow the patients breathing capacity, partly by clinical evaluation, and partly by following the decrease in vital capacity.

Equipment for oral intubation and positive pressure ventilation with either a bag and a mask, or a bag connected to the tube, were kept beside each bed as well as means of suction.

Sudden vomiting with aspiration could alter the situation in a few seconds, and make the use of the equipment necessary. A spare set of this equipment was kept ready on each floor, in case of failure of a patient's own set. This precaution has more than once proved to be lifesaving.

Talking about this equipment — necessary to perform an artificial emergency-respiration, and suction too, — it ought to be mentioned, that it should be available within a reasonable time to every patient in respiratory trouble — even in their own home. During the polio epidemic, it became the principle, that this help had to come to the patient, and not the patient to the help. Thus we went out in the country by ambulance or by plane and made many patients transportable before they were transported.

By this means transportation could be done safely.

This active approach to the problems of transportation, had developed by tragic experiences from patients left alone with an incompetent nurse or their mother, in an ambulance on its way to the hospital from far away. Aspiration in an ambulance driving 60 miles an hour is an easily provoked and often killing procedure. At the arrival to the hospital, many patients were found to be in a condition which made further treatment rather hopeless, — some were dead.

With adequate ventilation performed during the transportation, either through a tracheotomy, or through an oral tube, the outcome might have been a different one.

In the observation-department the patients' condition, and the indications for the different types of treatment were evaluated. The following may be a rough guide to illustrate the line which was followed.

Patients were divided into wet and dry cases, according to the amount of secretion in the airway. They were also divided into a group, where the respiratory muscles seemed to be able to perform an adequate exchange when a free airway was present, — and a group who were thought not to be able to do so.

The dry cases — with sufficient ventilation — very few in number — were just observed.

The dry cases with insufficient ventilation, were most often put in a tank or Cuirass-respirator, in order to give them a chance to get through without a tracheotomy. Only too often this was not possible. I only remember 2 patients, who were put dry in a tank, and remained dry.

The wet cases who seemed to have sufficient muscle power to maintain an adequate exchange, were put in postural drainage. We tried to keep the airway free, but very often a tracheotomy had to be done, in order to maintain a free airway. This was especially the case in some children, where cooperation for suction was little, and the drainage position difficult to maintain.

The wet cases with insufficient ventilation, had tracheotomy immediately, and were put on artificial respiration, which most often — at least in the first days, had to be given through the tracheotomy tube.

As a main rule — we did not dare to put wet cases in respirators, without a proceeding tracheotomy. The few times we tried so, we always regretted it.

In many cases where we were in doubt, whether the impaired respiration was mainly due to secretions, or to decreased ventilatory muscle power, we did a tracheotomy. When the airway was made free as well as possible, it was then decided, whether the patient could be left in postural drainage, or had to have artificial respiration. Most patients had to have the latter.

The choice of anæsthesia for the tracheotomies was a difficult one. Pentothal and scoline were used in the beginning, but were given up after one emergency, with a standstill of the heart in a patient in a tank-respirator. I am not sure, this was fair to the method. We got the heart started by heart-massage, and the patient recovered so much that she seemed to have pain that afternoon — but she died the following night, due to blocking of the tube by secretions from a many days old complete atelectasis of the left lung.

Later on cyclopropane was used. No premedication was given. Very often the patient stopped spontaneus breathing as soon as oxygen was given

— and had to be anaesthetised by squeezing the cyclopropan down into the lungs.

The tracheotomy performed was a high one, in order to stabilise the tube as much as possible in the trachea. A special device to maintain the tube in place, was invented by one of the E. N. T.-surgeons.

The tube was changed, when it was felt necessary. For practical reasons it was not possible to arrange a regular change. To our surprise however, these rubber-tubes, gave rise to very little local irritation in the trachea.

The first hour after the tracheotomy was always a very difficult one. The reflexes could be rather vigourous and pulmonary oedema could occur. We were rather afraid of giving intravenous fluids during this time, before the tube were quite in place.

The manual artificial respiration was done with a to and fro absorber-system with a flow of 5 l. pr. minute and a mixture of 50 % nitrogen and 50 % oxygen. Since we had to use medical students, it was felt that this system had some buffer-effect:

CO_2 excess could not develop if the absorber did not work.

Oxygen poisoning was not likely to occur.

Oxygen surplus was given to help in shock and pulmonary complications.

The high flow secured against low oxygen due to rebreathing.

No trouble with valves.

Drying out of the mucous membranes was propably not a problem as long as condensed water was present in the breathing bag.

Most of the patients had a stomach-tube passed through the nose just after the admission to the observation-ward. The tube was left in place in patients, who could not swallow. Food was given this way.

Paralytic ileus was a common complication, which made the stomach-tube a most valuable therapeutic measure in order to release the pressure on a weak diaphragm.

The cuffed rubber-tube in the tracheotomy was replaced with a silver-cannula as soon as possible. The E. N. T.-man decided when, by following the patients' capability of swallowing. This we learned to respect. In some patients, who were doing fine on their own spontaneous respiration, the change was done too early. The patients got atelectasis due to aspiration, and had to fall back into artificial respiration for weeks.

By working along these lines briefly mentioned, it was possible to improve the results. Naturally we ran into a lot of complications. Work was done in order to follow the patients with laboratory investigations of many kinds in order to estimate the proper ventilation, and to evaluate the shock mechanism. In this respect it was tried to give an artificial ventilation, which interfered as little as possible with the circulation. In order to accomplish this we had valuable help from Dr. C. G. Engström from Stockholm who worked with us. In a respirator which he has constructed it is possible to ensure that a certain volume of air is given with a lower mean mask pressure than in the devices where only positive pressure is used.

It was amazing however to see how the result could be improved by a very simple technic familar to all anaesthetists, and it is fair to conclude, that as soon as a patient is in trouble in a respirator he should — if the trouble can not be corrected — have help by other means. In Copenhagen it was artificial respiration through a cuffed tube inserted through a tracheotomy. The technic of performing this artificial respiration manually or mechanically can always be discussed and improved. But by the very simple technic used in Copenhagen, it was possible, when catastrophy struck, that every single patient who needed artificial respiration, could be treated.

SUMMARY

A review of the improvements in the treatment of acute bulbar poliomyelitis which were carried out in an emergency situation during the epidemic in Copenhagen 1952 has been presented. The use of a tracheotomy technique with the insertion of a cuffed endotracheal tube before the tracheotomy, and later on a cuffed tube through the tracheostoma, allowing assisted or controlled intermittent positive pressure ventilation, is recommended.

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THE EPIDEMICS OF ACUTE ANTERIOR POLIOMYELITIS IN DENMARK IN 1952 AND 1953

By HENRY HAMTOFT

The epidemics of poliomyelitis which struck Denmark in the years 1952 and 1953 may be classified as the largest polio epidemics in Denmark, since the first appearance of polio in this country about 50 years ago. The epidemic in 1952 was the largest hitherto observed and comprised a total of 5,676 cases of which 2,450 were paralytic, while the epidemic in 1953 involved 1,602 cases of which 684 were paralytic.

From Figure 1, which shows the occurrence of the disease in Denmark from 1934 (the year of the great epidemic) to 1953 (calculated per 100,000 population) it appears that the epidemic in 1953 similarly belongs to the greater epidemics as it is only surpassed by the epidemics of 1952, 1934 and 1944.

If the curve of the epidemic is followed through the two years, a minimum is observed about May 1st 1953. The following calculations

From the National Health Service.

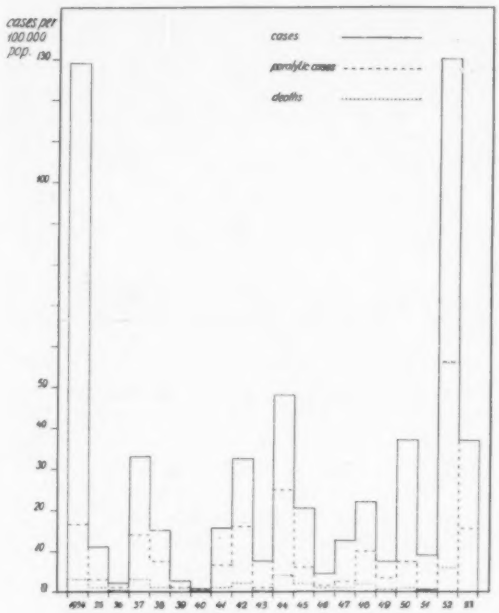


Fig. 1

are therefore mainly carried out so that the cases in the first 4 months of 1953 are grouped with the cases in 1952 while the cases after May 1st, 1953, are recorded separately.

The extent of the epidemic in 1952 was of such an order that an accurate record concerning the patients was desirable. Furthermore the National Health Service was aware of the fact that both in hospitalized patients suffering from poliomyelitis and in patient not admitted to hospital, cases of paralysis had occurred at such a late stage in the disease that they had escaped recognition and treatment. Therefore the National Health Service required in a circular of December 1952 that public health officers and hospitals should re-notify all cases of poliomyelitis and notify all cases of subsequent paralysis.

General practitioners were required through an announcement in the Danish Medical Journal (Ugeskrift for Læger) to re-notify all cases of poliomyelitis, previously notified as aparalytic, in which paralyses were later revealed and to notify all paralytic cases, not previously notified. This was done to ensure the recognition, continued control and adequate effective follow-up treatment of all cases with not only severe but also slighter paralysis and to render possible a reliable medical statistical account of the total number of cases of poliomyelitis and their distribution in various parts of the country, age groups etc.

The re-notification was effected by completion of special index cards which are now part of a Central Card-Index which serves the association for the care of disabled and the association against infantile paralysis respectively (Samfundet og Hjemmet for Vanføre and Landsforeningen mod Børnelammelse) as a basis for the follow-up treatment.

Similarly, in August 1953, the National Health Service required special index cards concerning all hospitalized patients to be forwarded.

The account in the present paper is based upon the re-notifications for 1952 and the notifications for 1953, corrected by the hospital cards.

The account was undertaken for both paralytic and aparalytic cases. Although it appears that there is a certain connection between the number of paralytic and aparalytic cases in the separate counties, this agreement was, however, not considered great enough to justify the inclusion of the aparalytic cases in the present statistics apart from an account of their occurrence as regards time and place.

The account concerns the Metropolitan area and the remainder of the country, each treated separately. The heading »Metropolitan area« includes in this connection the Boroughs of Copenhagen and Frederiksberg and the county district of Copenhagen (Northern and Southern Medical Districts, comprising the suburban boroughs of Copenhagen).

Figure 2 shows the weekly number of paralytic and aparalytic cases distributed in the two regions, recorded graphically. It appears clearly that the epidemic in 1952 started earlier and culminated earlier in the Metropolitan area and also ceased earlier there.

In 1953, there was no epidemic in the area of the capital. In the provinces, the epidemic commenced approximately at the same time as in 1952, although somewhat more widely spread, and until the middle of August 1953, the number of cases notified weekly exceeded those for 1952. Thereafter, the epidemic subsided rapidly and already at the beginning of September the weekly number of cases had fallen to half of the corresponding figures for 1952. By the end of the year the epidemic had ceased.

Table I and Figures 3 and 4 show the distribution of the cases in the Metropolitan area and the remainder of the country for the periods January 1952 — April 1953 and May 1953 — December 1953 respectively and for both periods taken together.

The number of paralytic cases per 100,000 population is considerably greater in the Capital (106) than in the remainder of the country (41). Bornholm is the county most affected (148), succeeded by the county district of Copenhagen (135). No consideration has in this connection been taken of the fact that the age distribution in the latter district differs somewhat from that in the remainder of the country, as in these boroughs where particularly many newly married couples have settled, numerous children are encountered. The lowest incidence of polio-

TABLE I.

Acute Anterior Poliomyelitis in Denmark 1952 - 1953.

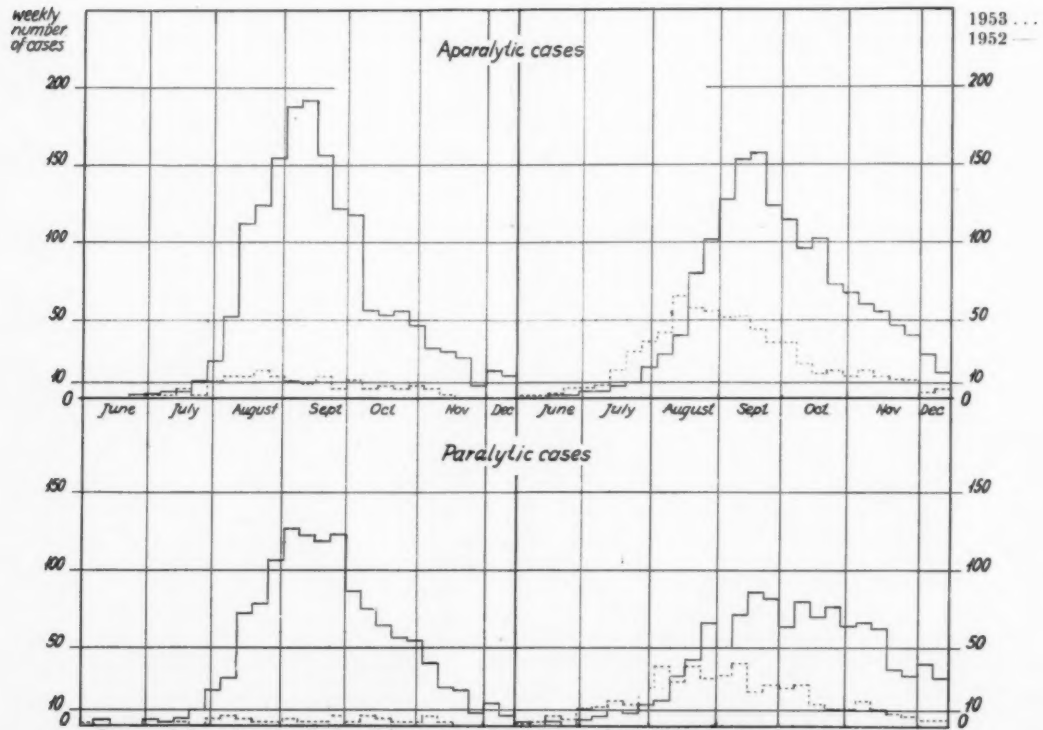
	Jan. 1952 - April 1953				May 1953 - Dec. 1953				1952 + 1953 paralytic cases per 100,000 population
	paralytic cases		aparalytic cases		paralytic cases		aparalytic cases		
	total	per 100,000 pop.	total	per 100,000 pop.	total	per 100,000 pop.	total	per 100,000 pop.	
Metropolitan area	1289	106	1631	134	53	4	147	12	110
Rest of the country	1271	41	1694	55	521	17	672	21	58
Total Denmark	2560	58	3325	76	574	13	819	19	71

myelitis in 1952 occurred in Jutland, particularly South Jutland, where in the county of Tønder not a single case was registered.

In 1953, the picture changed completely. The counties which showed the greatest number of cases in 1952, practically escaped the epidemic in 1953, while the counties, not stricken by the epidemic in 1952 showed large numbers of cases in 1953. The counties of Randers and Ringkøbing constitute exceptions as they had relatively numerous cases in both years compared with the other counties in Jutland. The county of Ringkøbing was so heavily afflicted in 1953 that the total number of cases for both years together was greated than anywhere else in the counties outside the capital, except for the county of Roskilde.

There thus exists a definite negative correlation between the incidence of poliomyelitis in the two years. If the figures for the 2 years be added up, the difference becomes thus distinctly less, but it is, not ruled out entirely. Thus only two of the counties in Jutland show figures above the average for the provinces and only two districts on the islands figures below the average.

Tables IIa and IIb show the distribution of the paralytic cases according to age and sex within the Metropolitan area and the remainder of the



Metropolitan area. Fig. 2 *Remainder of the country.*

TABLE II.

Acute Anterior Poliomyelitis in Denmark.
Paralytic cases.

II a. January 1952 - April 1953

Age groups	No. cases notified						No. cases per 100,000 population					
	Metropolitan area		Remaining country		Total		Metropolitan area		Remaining country		Total	
	M	F	M	F	M	F	M	F	M	F	M	F
Under 1 year	26	24	20	20	46	44	270	264	68	72	118	119
1 —	90	61	54	51	144	112	923	659	190	189	377	309
2 years	88	59	63	71	151	130	935	663	210	249	384	348
3 —	63	45	50	43	113	88	670	506	167	151	287	235
4 —	60	38	51	41	111	79	585	390	154	134	255	196
5 —	57	39	56	25	113	64	504	359	168	77	253	148
6 —	40	31	41	37	81	68	345	274	117	108	173	150
7—9 —	59	50	87	56	146	106	182	159	90	60	113	85
10—14 —	43	28	51	38	94	66	106	71	40	30	55	40
15—19 —	21	46	45	47	66	93	60	135	38	42	44	64
20—24 —	21	40	41	44	62	84	60	94	38	44	43	59
25—29 —	41	63	39	51	80	114	95	130	37	49	54	75
30—44 —	65	82	69	59	134	141	48	52	21	18	29	29
45—	5	4	12	9	17	13	3	2	2	2	3	2
Total	679	610	679	592	1358	1202	120	95	43	38	63	55

II b. May - December 1953

Age groups	No. cases notified						No. cases per 100,000 population					
	Metropolitan area		Remaining country		Total		Metropolitan area		Remaining country		Total	
	M	F	M	F	M	F	M	F	M	F	M	F
Under 1 year	2	—	10	3	12	3	21	—	34	11	31	8
1 —	1	2	29	23	30	25	10	22	102	85	79	69
2 years	2	—	28	28	30	28	21	—	94	98	76	75
3 —	2	—	25	20	27	20	21	—	83	70	69	54
4 —	2	2	17	14	19	16	20	21	51	46	44	40
5 —	3	2	14	12	17	14	27	18	42	37	38	33
6 —	—	—	18	14	18	14	—	—	51	41	39	31
7—9 —	3	4	22	27	25	31	9	13	23	29	19	25
10—14 —	2	1	27	20	29	21	2	3	21	16	17	13
15—19 —	—	6	11	23	11	29	—	18	9	21	7	20
20—24 —	1	1	16	17	17	18	3	3	15	17	12	13
25—29 —	4	2	20	9	24	11	10	4	19	9	16	7
30—44 —	7	3	38	25	45	28	5	2	12	8	10	6
45— —	—	1	7	4	7	5	—	1	2	1	1	1
Total	29	24	282	239	311	263	5	4	18	15	14	12

country, together with the number of cases per 100,000 population in these groups, calculated separately for the two periods treated.

It appears, that the age group most afflicted is that from 1 to 3 years. In the region of the capital, in 1952, one per cent. of boys between 1 and 3 years of age suffered from paralytic infantile paralysis. For 1953, the figures are small, but the relation between the figures for the separate age groups in the 2 years is fairly similar for all age groups. In the provinces, in 1953, there were half as many cases as in 1952 and this holds true, by and large, for all age groups, perhaps with the exception of the age group 4—10 years, in which the number of cases in 1953 fell slightly short of that anticipated.

Table II shows further, that males were affected to a greater extent than were females in so far as the incidence is highest in boys to the age of 15 years while females are most affected in the age group 15—30 years. In older age groups, the incidence is practically equal. Adults over 45 years practically escaped poliomyelitis. 70 per cent. of all paralytic cases were in children under the age of 15 years and this corresponds to the average figure for the last 10 years.

Table 3 shows the mortality in 1952 alone, as the number of deaths due to poliomyelitis in 1953 has not yet been calculated. A total of 262 deaths due to infantile paralysis occurred in 1952.

Table 3 shows for 1952 both the *mortality* (number of deaths per 100,000 population) and

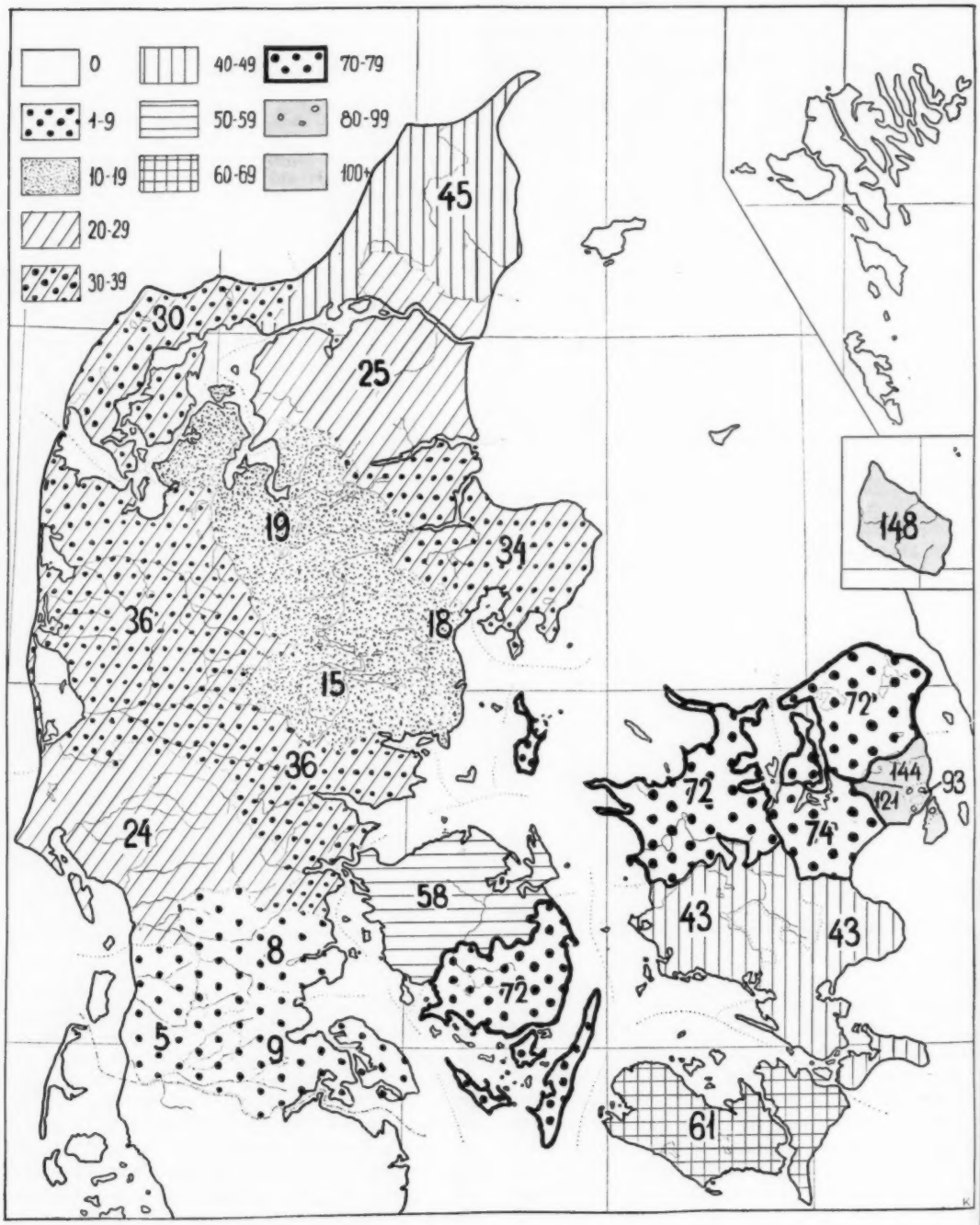


Fig. 3. *Poliomyelitis ant. ac. paralytica in Denmark Jan. 1952—April 1953. (No. of cases per 100.000 population).*

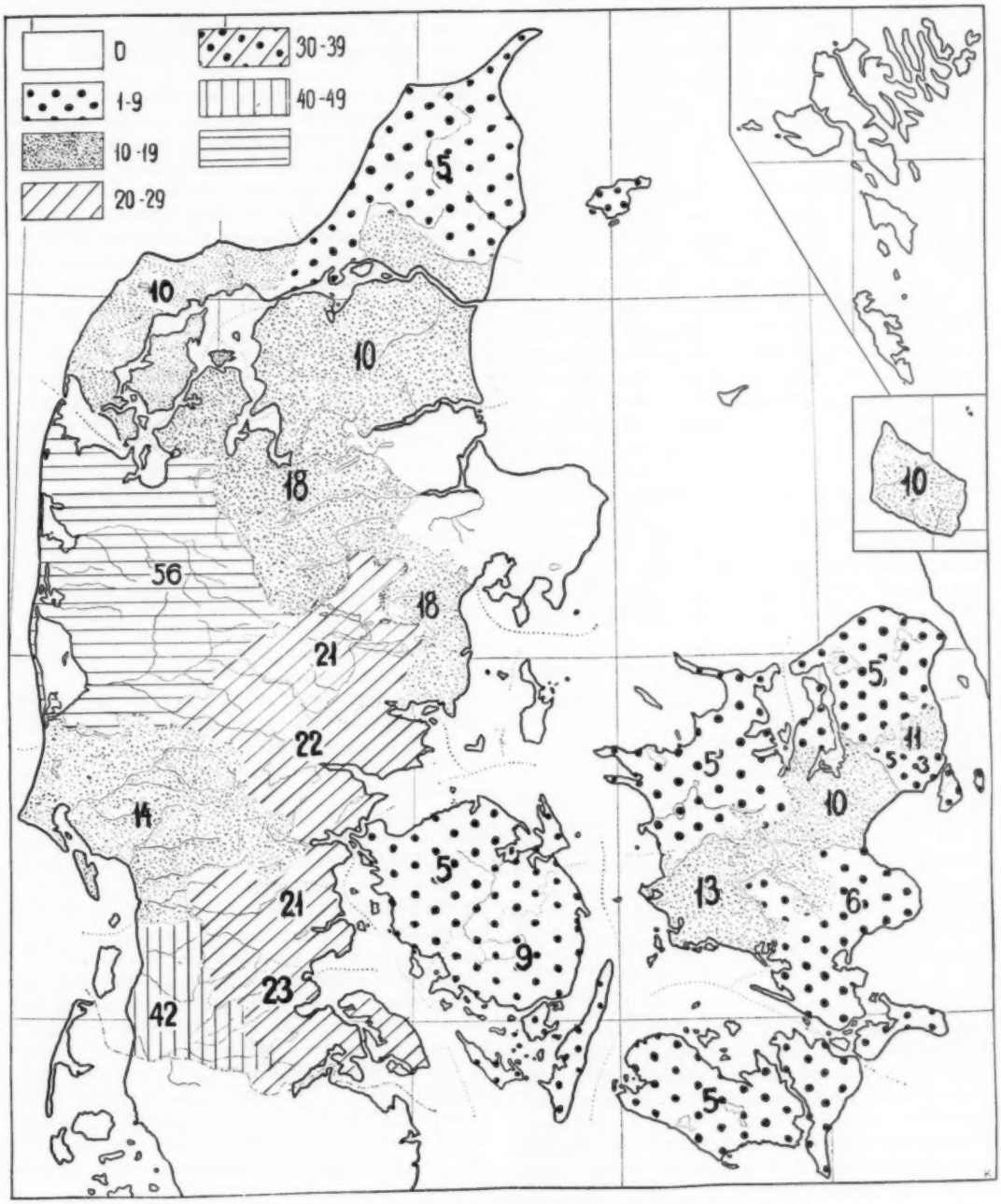


Fig. 4. *Poliomyelitis ant. ac. paralytic in Denmark May—December 1953.*
(No. of cases per 100.000 population).

TABLE III.
Acute Anterior Poliomyelitis 1952.

Age groups	Metropolitan area M.	Metropolitan area F.	Remainder of country M.	Remainder of country F.	Entire country M.	Entire country F.
			Deaths*).			
Under 1 year	2	2	5	2	7	4
1— 4 years	20	6	22	14	42	20
5—14 »	11	9	27	12	38	21
15—64 »	34	19	41	34	75	53
65 years and over	1	—	1	—	2	—
Total	68	36	96	62	164	98
			Deaths*) per 100,000 population (mortality).			
Under 1 year	19,8	22,0	17,1	7,2	18,0	10,8
1— 4 years	51,5	16,3	18,3	12,2	26,4	13,2
5—14 »	11,4	9,7	9,2	4,2	9,7	5,6
15—64 »	8,9	4,3	4,1	3,5	5,4	3,7
65 years and over	2,3	—	0,7	—	1,1	—
Total	12,0	5,6	6,0	4,0	7,6	4,5
			Paralytic cases.			
Under 1 year ...	25	24	15	17	40	41
1— 4 years ...	300	203	210	192	510	395
5—14 » ...	198	147	219	143	417	290
15—64 » ...	150	232	178	195	328	427
65 years and over	1	—	1	—	2	—
Total	674	606	623	547	1297	1153
			Deaths*) per 100 paralytic cases (fatality).			
Under 1 year ...	8,0	8,3	33,3	11,8	17,5	9,8
1— 4 years ...	6,7	3,0	10,5	7,3	8,2	5,1
5—14 » ...	5,6	6,1	12,3	8,4	9,1	7,2
15—64 » ...	22,7	8,2	23,0	17,4	22,9	12,4
65 years and over	100,0	—	100,0	—	100,0	—
Total	10,0	6,1	15,4	11,3	12,6	8,6

*) Deaths in 1952 only.

the *case fatality rate* (number of deaths per 100 notified paralytic cases). It appears, that the lethality is greatest among adults, less among females than among males and less in the capital than in the remainder of the country. 50 per cent. of the deaths occurred in children under the age of 15 years and this corresponds to the experience during recent years.

There is a slight tendency to lower lethality in those counties (Bornholm excepted) where the morbidity is greatest (viz. more than 60 paralytic cases per 100,000 population). The cause of this cannot be elucidated without deeply penetrating investigations.

No cases of infantile paralysis occurred in 1952 and 1953 in the Faroe Islands.

PROLONGED TREATMENT OF RHEUMATOID ARTHRITIS WITH CORTISONE

By FINN FISCHER, BENT HARVALD and KNUD BRØCHNER-MORTENSEN

Following the report of Hench, Kendall, Slocumb and Polley (6) on the effect of cortisone and ACTH in rheumatoid arthritis, it soon became apparent that this effect lasts only as long as the preparations are administered and that the treatment scarcely increases the frequency of remissions above the number of spontaneous remissions anticipated (i. e. approx. 10 per cent.), even when large doses are administered. The problem which consequently presented itself was whether it might be possible to carry out prolonged treatment with a maintenance dose of such an order that, on the one hand, a reasonable reduction in the symptoms of the disease was obtained while, on the other hand, side-effects and complications were reduced to a minimum. Recently, a number of communications have been published concerning the results of treatment, carried out over a prolonged period, in certain cases amounting to several years (1, 2, 3, 4, 5, 7, 8, 9, 11, 12). From these communications it appears, that such a treatment may be carried out in a number of patients with satisfactory results, but comparison is difficult as the criteria, employed in selecting the patients, vary somewhat in the various materials.

In the following, the results of prolonged treatment of the first 50 patients who underwent such a treatment in Medical Department A, the University Hospital (Rigshospitalet), Copenhagen, are presented.

The material comprises 15 males and 35 females, the majority of whom were in the age group of 30—50 years. All presented typical clinical pictures. Two were in the first stage, 15 in the second stage, 18 in the third stage and 15 in the fourth stage of the disease, i. e. severe cases preponderated. In all cases, the disease was in an active, progressive phase. At the time of commencement of treatment, the duration of illness varied between 3 months and 22 years; 36 patients had been ill for more than 2 years; 21 out of these for more than 5 years. The average duration was approximately 6 years. All patients had previously been treated according to the conventional principles and the majority had received gold treatment, frequently several courses.

For experimental reasons, the treatment was initiated with ACTH in all cases; subsequently, the treatment was continued virtually exclusively with cortisone. No other kind of treatment was provided apart from that necessary in manifest complications. With the exception of simple,

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active exercises, all physiotherapy was discontinued and analgesics were avoided as far as possible. In 3 patients, however, arthroplastic operations was performed on anchylosed knee joints as part of the treatment.

As appears from Table 1, which as the other tables records status as per February 1, 1954, treatment was discontinued in 9 patients on account of unsatisfactory response (Group A) and in 6 patients on account of undesirable side-effects (Group B). In 5 patients (Group C), treatment was discontinued on account of remission, which persisted at the time of the analysis of the material. In the remaining 30 patients (Group D), treatment was continued.

Table 1:
50 Patients with Rheumatoid Arthritis Treated with with ACTH and/or Cortisone.

Group A: Treatment discontinued (unsatisfactory response)	9
— B: Treatment discontinued (complications)	6
— C: Treatment discontinued (remission)	5
— D: Treatment continued	30

The duration of treatment in the various Groups appears in Table 2. All patients in Group D underwent treatment for over one year and in isolated cases for 40 months, as a maximum.

Table 2:
Duration of Therapy

Months	Total number of patients	Group A	Group B	Group C	Group D
2— 6	7	4	2	1	0
6—12	3	1	0	2	0
12—24	35	4	3	2	26
24—36	2	0	0	0	2
36—40	3	0	1	0	2
	50	9	6	5	30

The maintenance doses in the 30 patients in whom treatment was continued appear in Table 3. The majority of patients were treated with 62.5—75 mg. cortisone orally dialy.

Table 3:
Maintenance Dose, February 1, 1954.

Cortisone 87 mg	3 patients
— 75 mg	17 —
— 62 mg	7 —
— 50 mg	2 —
— 37 mg	1 —

In evaluating the results of treatment in the total material according to the criteria, recomended by the American Rheumatism Association (10), considerable improvement (Grade 2) was found in 20 patients; some improvement (Grade 3) in 18 and no improvement (Grade 4) in 12.

The patients' capacity for work prior to treatment compared with their capacity for work at the time of the analysis or the time of final discontinuation of treatment appears in Table 4. Among the 35 patients where treatment was continued or (temporarily?) discontinued on account of remission, the number of those with capacity for work increased from 2 to 24 while the number of totally incapaciated fell from 8 to 1; in 3 out of these latter patients, the improvement is, however, partially attributable to supplementary arthroplastic operation upon the kneejoints.

Table 4:
Capacity for Work Before and During Therapy.

Class	Group A before/ during therapy	Group B before/ during therapy	Group C before/ during therapy	Group D before/ during therapy
I (complete ability) ..	0/0	0/0	0/0	0/0
II (adequate ability) ..	0/0	0/1	1/4	1/20
III (limited ability) ...	3/3	6/4	3/1	22/9
IV (incapacitated)	6/6	0/1	1/0	7/1
	9	6	5	30

During treatment, various side-effects were observed in the majority of patients (Table 5). In the great majority of cases, symptoms are encountered which admittedly are undesirable but hardly are of grave significance (moon-face, moderate increase in weight etc.). In 9 patients,

Table 5:
Complications During Treatment with ACTH and Cortisone.

	Complications in the total number of patients treated (total no. 50)	Complications in patients in whom cortisone treatment is in progress (total no. 30)
Moon-face	48	27
Fatpads	3	2
Increase in weight	32	24
Hirsutism	6	3
Acne	4	0
Pigmentation	2	0
Menstrual disturbances	5	0
Mental disturbances (depression)	7	1
Mental disturbances (euphoria)	3	3
Glycosuria	9	0
Halisteresis	0	0
Elevation of blood pressure	13	7
Dilatation of the heart	16	15
Oedema	7	0
Hypopotassaemia	7	0
Electrocardiographical changes	6	1
Perforated ulcer	1	0
Activated ulcer	1	0
Secondary infection	4	0
Abscess	4	0
Delayed wound healing	4	1
Ecchymoses	6	0
Paraesthesia	2	0

slight, transient glycosuria was observed during the initial treatment with ACTH.

Mental disturbances occurred in a total of 10 patients and caused discontinuation of treatment in 4; no permanent changes were, however, observed.

Slight elevation of blood pressure was observed in 13 patients, in the majority of whom the blood pressure was near the upper limit of normal at the commencement of treatment.

Radiologically demonstrable enlargement of the heart was found in 16 patients, the order of which varied somewhat from one examination to another but was always moderate. In isolated cases, transient electrocardiographic changes in connection with hypopotassaemia were encountered during the initial treatment with ACTH and a number of patients complained now and again of palpitations. Apart from this, no sign of cardiac nor renal affections was found. During early treatment, the changes in the fluid and electrolyte balance, well known from the literature, were encountered and, in isolated cases, oedemata, but frequent control examinations during the continued treatment with cortisone revealed normal conditions.

In two of the patients, fractures occurred during the period of observation, but on both occasions in connection with adequate injuries. Severe halisteresis was not revealed on radiological control in any case. There were no thromboembolic phenomena.

A number of patients complained of slight dyspeptic symptoms, most frequently hunger pain, as a transient phenomenon. In one patient an ulcer, the presence of which was previously verified, was activated and in another patient, with no previous ulcer symptoms, perforation of a gastric ulcer occurred; operation was performed with good result.

Delayed healing of wounds was observed in a total of 4 patients; secondary infections similarly in 4, one of whom developed pneumonia. Repeated radiological control examinations showed no signs of activation of pulmonary tuberculosis.

In association with a minor surgical intervention, one patient developed serious symptoms of insufficiency of the adrenal cortex shortly after erroneous discontinuation of treatment.

According to our preliminary experience, we consider ourselves justified in concluding that prolonged treatment with cortisone has proved valuable in the majority of patients in the present group.

In view of the risk of side-effects, treatment should be instituted only after meticulous deliberation of indications and contraindications and the patients should be observed closely during the entire period of treatment. ACTH and cortisone should not be employed in very early and fairly inactive cases af rheumatoid arthritis; in the slightly more active stages gold therapy should, as a rule, be attempted. Indications are primarily present in cases where the disease progresses despite other types of treatment but occasionally the treatment must be considered indicated as the primary one in particularly markedly active or rapidly progressive cases in order to attempt to inhibit the progression before irreversible joint changes occur.

In far advanced cases, the results will, as a rule, not outweigh the risks and restraint should be exercised in the institution of hormonal therapy in elderly patients with coronary sclerosis and osteoporosis. Among the contraindications, the following should, in addition, be emphasized: active infections (particularly tuberculosis), hypertension, cardiac and renal insufficiency, gastric ulcer, mental instability and perhaps diabetes.

In establishing the maintenance dose, regard should be paid to the patient's tolerance rather than to the complete suppression of the symptoms of the disease. During treatment, the patients should undergo regular control examinations and this holds particularly true if the treatment be discontinued; treatment ought always to be discontinued gradually on account of the risk of insufficiency of the adrenal cortex.

SUMMARY

The results of prolonged treatment with cortisone in 50 patients with rheumatoid arthritis are reported. The treatment was discontinued on account of unsatisfactory response or complications in 9 and 6 patients, respectively, and on account of remission in 5. In 30 patients, the treatment was continued for 12 to 40 months; out of these 30 patients, only one was capable of work prior to institution of treatment as compared to, 20 at the time of analysis of the material.

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ADMINISTRATION OF VITAMIN K ANTE PARTUM

PROPHYLAXIS AGAINST HAEMORRHAGIC DISEASE OF THE NEWBORN

By P. PLUM, H. DAM, H. DYGGVE and E. HJALMAR LARSEN

Between 1939 and 1940 several authors (4, 10, 16, 26) independently reported the existence of a relationship between vitamin K and haemorrhagic disease of the newborn. It was found (14, 24) that administration of vitamin K to mothers during the last days of pregnancy prevented the usual decline of prothrombin activity of the infants' blood during the days immediately after birth. The problem of the prophylactic value of vitamin K against haemorrhagic disease of the newborn was thereby raised. Opinions have varied from great enthusiasm to complete denial of the value of such a measure. (1, 7, 9, 11, 15, 17, 19, 21, 22). In the following, we shall summarize our experience in this question, which is also of importance in relation to the prophylaxis of cerebral palsy.

As regards the prothrombin activity at birth and its variations in the early period of postnatal life there seems to be general agreement on the following points:

1) The prothrombin activity of the infant at birth is lower than that of infants a few weeks old, which again is lower than that of children one year old and than that of adults.

2) The variation of prothrombin activity during the first week of extra-uterine life follows a characteristic course. During the first two to four days prothrombin activity declines to a varying degree and during the latter half of the first week it increases to a level which is generally higher than that at birth. From then on, the increase is slower until a constant level, identical with that of normal adults, is reached at the age of about one year (18).

3) This course is characteristic of normal breast-fed infants, whereas in artificially fed children the decline of prothrombin activity in the first week is usually not found (13, 20).

4) Administration of vitamin K, either to the child or to the mother shortly before or during labour will increase the prothrombin activity of the blood of the child in the days after birth.

Thordarson (25) and Larsen (13) showed that the infant's prothrombin activity at the moment of birth was usually between 20 % and 50 % of the normal adult value. In contrast to the postnatal decline of prothrombin activity this value at birth is largely uninfluenced by antenatal administration of vitamin K (Larsen (13)) and is thus not due to lack of this vitamin.

It is of particular interest in relation to the problem of haemorrhagic disease of the newborn that extremely low prothrombin activity may be found at the moment of birth. Larsen (13) found such low values, down to a few per cent of the normal adult activity, in infants who suffered from intra-uterine asphyxia to the extent that the amniotic fluid was discoloured by meconium.

At present, there is no obvious explanation of the moderately decreased prothrombin activity at birth. The most likely explanation of the decline and following rise of the prothrombin activity of breast-fed infants in the first week is that not until the third to fourth day when the milk »comes in«, is the supply of vitamin K through the milk sufficient to ensure a synthesis of prothrombin high enough to exceed or equal its metabolic destruction. The content of vitamin K of breast milk is low (3, 23) but apparently adequate to meet the infants' requirements at the time when the milk supply is otherwise sufficient. The requirement of vitamin K during the first week after birth has been found experimentally to be only about 10 micrograms daily (8, 13, 23).

Regarding the question whether there is any causal relationship between low prothrombin activity and appearance of haemorrhage, it must be remembered that bleeding is always initiated by a vascular lesion. It may, therefore, not follow, *a priori*, that every infant with low prothrombin activity will show signs of haemorrhage. That there will be more infants suffering from haemorrhage among those whose prothrombin activity is very low, than among those who have a higher prothrombin activity, appears from Table 1 (2).

Table 1.
Incidence of Haemorrhage and Prothrombin Content of the Blood).*

No. of infants	Prothrombin time. sec	Prothrombin, %	*Infants with haemorrhage* No.	%
969	100	7	53	5
178	300	3.5	23	13
25	1,000	2.5	9	36

*) Prothrombin time was estimated at the time of bleeding in infants with haemorrhage and at the age of 2 to 4 days in infants without haemorrhage.

The question whether prophylactic administration of vitamin K to mothers lowers the incidence of haemorrhage in the newborn was investigated by Dyggve (5, 6). A summary of his results is presented in Table 2.

This table shows that the characteristic manifestations of haemorrhagic disease of the newborn, viz. melaena and umbilical bleeding, are considerably less frequent in the vitamin K treated group. Thus, it is evident that administration of vitamin K to the mothers is of definite prophylactic value.

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Table 2.
Incidence of Haemorrhagic Manifestations in Newborn Infants).*

Type of haemorrhage	No. of cases per 10,000 Vitamin K to mothers**)	No vitamin K to mothers
Melaena	6	16
Umbilical	1	9
Adrenal	5	15
Subcapsular hepatic	12	18
Intraperitoneal	2	8
Cutaneous	20	23
Cephalhaematoma	105	111
Intracranical	123	163

*) The series comprises 10.876 infants whose mothers received vitamin K, and 22.371 infants whose mothers were not given vitamin K.

**) Administered 1 to 24 hours before delivery. About 4,350 mothers received Synkavit (10 mg intramuscularly), about 3,000 mothers received Synkavit (20 mg orally), about 2,700 received the disuccinate (2,000 received 10 mg orally, and 700 20 mg orally), while about 700 mothers received the sulphate of 2-methyl-1,4-naphthohydroquinone in 10 or 40 mg doses orally or intravenously.

The internal haemorrhages (adrenal, subcapsular hepatic, intraperitoneal and intracranical) also occur less frequently in the treated group. Since these internal haemorrhages are numerically more important and prognostically graver, this difference is noteworthy. A closer analysis of the group of intracranical haemorrhage revealed (5) that the difference in frequency was considerably greater in premature infants than in full term infants. This may indicate that vitamin K prophylaxis will decrease the frequency of intracranical haemorrhage, especially in premature infants. As previously mentioned, anoxia predisposes to low prothrombin activity; since anoxia also tends to increase capillary fragility, the fact that intracranical haemorrhages are frequent in asphyxiated prematures may be explained as a result of coincidence of these two factors. It is evident, however, that other factors also play a role in the etiology of haemorrhagic manifestations of the newborn. Thus, besides mechanical factors, a seasonal variation in the frequency of intracranical haemorrhages has been found (2, 5, 12). This variation was most marked in premature infants (5). The seasonal difference seems to be unrelated to the supply of vitamin K, since it was found both in the group where the mothers had received vitamin K before delivery and in the group without vitamin K prophylaxis.

The authors are of the opinion that vitamin K should be given prophylactically as a routine measure to all mothers just before or during labour, since it is impossible to decide beforehand in which cases this measure will be of decisive importance.

Among the vitamin K preparations available we have found the tetrasodium salt (for intravenous use) or the dicalcium salt (for oral use) of 2-methyl-1,4-naphthohydroquinone-diphosphoric ester (Synkavit) suitable for the purpose. The therapy recommended is to administer 40 milligrams orally 48—4 hours before delivery. If vitamin K has not been administrered orally, 10 milligrams intravenously until 30 minutes before delivery will be sufficient*) If no vitamin K has been given to the mother prior to delivery, the infant should be given 5—10 milligrams intramuscularly immediately after birth.

With regard to statements in the literature denying the prophylactic value of vitamin K administration it should be emphasized that comparison between groups of treated and non-treated can only be made when the groups are sufficiently large and comparable. Confusion has arisen as a result of reports in which these conditions were not taken into consideration.

SUMMARY

A report on the value of *ante partum* administration of vitamin K as a prophylactic measure is given. The incidence of haemorrhagic disease of the newborn is shown to be significantly reduced in a large series of cases as compared with a similar series of non-treated controls.

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OXYURIASIS

DEMONSTRATION OF THREADWORM EGGS BY A NEW MODIFICATION OF THE ADHESIVE CELLOPHANE METHOD

By M. S. NORN

Numerous methods for demonstration of threadworm eggs have been suggested; the majority are, however, very unreliable. I have tried out a number of these methods (Hall's cellophane swab (4), Markey's anal swab concentration technique (5), Jacob's modification af Graham's adhesive-cellophane method (2) and analyses of the faeces (7)). As a result, I developed a new modification of the adhesive-cellophane method, probably the best method at present (6).

The procedure is the following: a strip of adhesive-cellophane approximately 5 cm. long is employed; it is placed around the end of a glass rod (Figure A) with the adhesive side outwards and held in position by the thumb and index finger of the investigator. With the end of the glass rod, thus covered with adhesive-cellophane, the patient's anal region is now carefully swabbed. The adhesive-cellophane may now be stuck on to a slide (B) and the preparation may be sent in this condition to the laboratory. Before microscopic examination can be undertaken, nearly the whole of the adhesive-cellophane must be detached from the slide (C) whereupon one or two drops of immersion-oil are placed in the fold between the adhesive-cellophane and the slide. The adhesive-cellophane is then replaced on the slide with a finger (D and E). In this way, a thin film of immersion-oil is formed between the adhesive-cellophane and the slide. The preparation is now ready for microscopic examination.

The advantages of the new modification, viz. employment of immersion-oil, are partly that the adhesive-cellophane optically disappears entirely from the preparation and partly that the threadworm eggs appear very distinctly in the prepa-

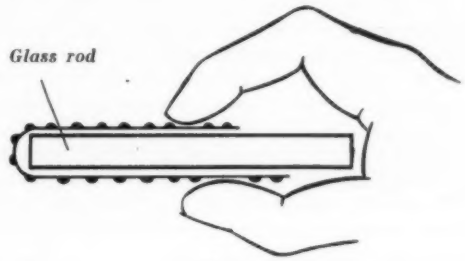

Fig. A.

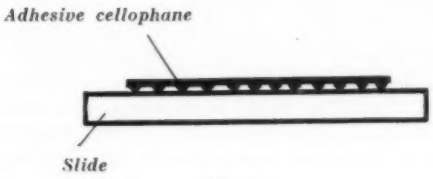

Fig. B.

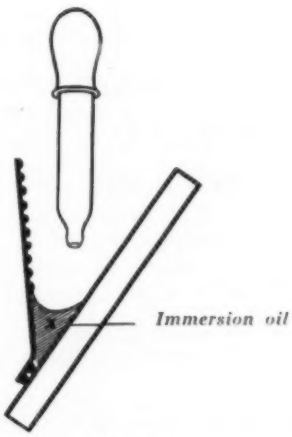

Fig. C.

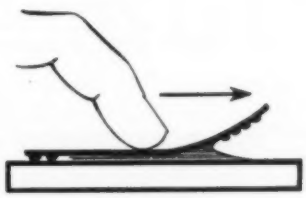

Fig. D.

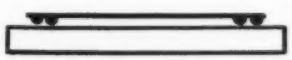

Fig. E.

ration, actually shining with a radiance of their own so that it is difficult to miss them even on quick microscopic examination under low power.

Based upon an investigation on over 600 individuals, I found that more than half of those infested with threadworms (58 per cent.) were disclosed by only one swabbing, 80 per cent. by two swabbings and 93 per cent. by 3 swabbings. To exclude the diagnosis of oxyuriasis with satisfactory accuracy (97—99 per cent.) at least 4—5 swabbings must be undertaken.

It is irrelevant whether the swabbings are undertaken early in the morning or later in the forenoon, while swabbing in the afternoon seems to give slightly inferior results.

OXYURIASIS: INCIDENCE AND SYMPTOMS

On examination of 609 individuals, chosen at random (children from institutions, conscripts and patients admitted to medical wards) with the adhesive-cellophane immersion-oil method (6) I found an incidence of oxyuriasis of 26 per cent. The majority of those infested were of school age (74 per cent.) with decreasing frequency towards higher and lower ages. The eldest patient was 78 years of age.

In a few cases only did oxyuriasis give rise to symptoms: pruritus ani (6.8 per cent. as compared with 5.1 per cent. in the control group) and irritation around the anal orifice (in 8.7 per cent. as compared with 3.3 per cent. in the control group).

No dyspeptic symptoms nor anaemia were encountered.

Address: St. Hedvig's Clinic, Kolding.

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PYELO-URETEROMETRY

APPARATUS AND NORMAL GRAPHS

By AUG. HALBORG SØRENSEN and M. ANDREASSEN

In attempts to record the changes of pressure in the upper urinary tract under normal and pathological conditions, the authors employed an apparatus, basicly complying with the principles indicated and applied by Tybjærg Hansen in recording the pressures in the heart and great vessels.

Few papers have previously been published on pressure measurements in the upper urinary tract. In 1932, Trattner described a hydrophorograph. With this apparatus he considered himself able to demonstrate obstruction in the ureter but he supplied no further information concerning more detailed reading of the curves recorded. In our opinion, Trattner's apparatus is not sufficiently sensitive to record the changes in pressure which take place in the upper urinary tract, particularly as he employed catheters of such a calibre for catheterization that the orifices of the ureters virtually were completely obliterated during measurement, a condition which must be considered unphysiological. Our apparatus consists of a manometer, constructed as a small chamber. The floor of the chamber functions as the one side of a condenser plate which is subjected to the pressure variations. In this way, the capacity of the condenser undergoes variations. These changes are amplified and the impulses are led to a mirror galvanometer which traces upon an electrocardiographic film. To record time, a distance between two vertical lines representing one second (see Figure 1) has been chosen.

The patient is placed horizontally with the manometer at the level of the symphysis. An inelastic ureter catheter is introduced through a cystoscope. When urine begins to flow from the catheter, this is connected with the manometer, previously filled with saline.

The ureter catheters employed are Neoplex 5—4, truncated at the tip so that the lateral aperture is removed. These catheters are so fine that they do not obliterate the orifice of the ureter.

By means of test pressures (vide infra) employed at the commencement and at the termination of the investigation, giving a constant amplitude on the graph, it can be ascertained that the ureteric orifice is patent.

In order to be able to convert the pressure variations, recorded in the graph, to absolute figures, a test device in connection with the apparatus is necessary. A container with fluid (physiological saline) is placed above the manometer at a certain level and is connected with the manometer. The manometer is fitted with a three-way cock which may be opened to the catheter, the atmospheric air and the fluid container, respectively. This makes it possible to fill the chamber of the manometer, to direct saline into the urinary passages and to produce test pressures. After filling the chamber with saline so that all air leaves the system, connection with the atmospheric air is established and a zero line may be

From the Surgical Department C (Professor *E. Dahl-Iversen,* M. D.), Rigshospitalet, University of Copenhagen and Dronning Louises Børnehospital, Copenhagen (Professor *Oluf Andersen,* M. D.).

recorded on the electrocardiographic film. Subsequently, the connection with the atmospheric air is closed and connection with the ureteric catheter is established. This procedure is immediately followed by an increase in pressure, attaining 20—30 cm. H_2O. This sudden increase in pressure probably originates from the pressure exerted upon the patient's renal pelves and ureters by the neighbouring viscera.

RESULTS

Pressure measurements were carried out in 60 patients, the majority of whom suffered from abnormalities or affections of the urinary tract. This number is small and does not permit the publication of a reliable standard graph of the normal pressure in pelvis and ureters but isolated characteristic findings should be pointed out at the present stage. In all cases, the graphs reveal the following types of oscillation:

1) Large oscillations, appearing at more or less regular intervals. The amplitude of these oscillations varies, but is in most cases of the order 40—60 cm. H_2O. In one patient, however, a pressure of 180 cm. H_2O was registered. The duration of these oscillations is about 1—2 seconds and their frequency approximately 1—16 per minute (Figure 1).

Fig. 1.

2) Pressure oscillations of much more rapid rhythm and of lesser amplitude. The pressure varies from a few cm. up to 10 cm. H_2O (Figures 1 and 3, at arrows). The cause of these oscillations is still obscure.

3) Quite small movements of a frequency of 300—400 per minute. The pressure variation is only a few mm. H_2O. These small movements probably originate from the undulations, transmitted from the adjacent arteries to the fluid in renal pelves and ureters (Figure 2).

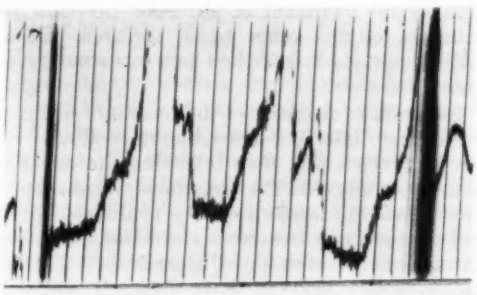

Fig. 2.

4) Finally, a number of oscillations appear on the graphs, which are due to movements of the patients, e. g. cough, deep respiration, straining of the abdominal muscles, micturition reflex and changes in position.

The apparatus allows for damping of the rapid, small oscillations, mentioned under 3. It is also possible to abolish the oscillations mentioned under 2, so that only the large pressure oscillations are preserved.

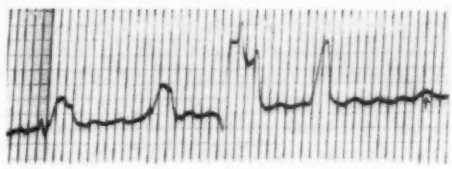

Fig. 3.

Figure 3 shows a graph where the catheter was first placed in the renal pelvis and subsequently slowly withdrawn into the ureter. It appears, that the contractions in the pelvis are less and more diffuse than in the ureter. The reason for this is presumably that the pelvic musculature has two layers in contrast to the ureteric musculature which has three layers.

SUMMARY

A preliminary report on pressure measurements in the renal pelvis and the ureter. Normal curves are presented and their interpretation is discussed.

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EPIPHYSEOLYSIS CAPITIS FEMORIS

A FOLLOW-UP EXAMINATION WITH PARTICULAR REGARD TO RESULTS OF TREATMENT AND SOCIAL PROGNOSIS

SUMMARY OF THESIS

By V. ORAM

During the years 1938—48, inclusive, approximately 600 cases of epiphyseolysis capitis femoris (ecf) were diagnosed in Denmark. 11.5 per cent. were missed at the first examination. 25 per cent. of the patients were treated in specialized departments and 75 per cent. in general hospitals. Socially, the majority of the patients belonged to the agricultural population, the remainder to the artisan, commercial and transport groups while only a few represented the professional classes. The sex ratio was 3 boys to 1 girl. Three quarters of the cases were unilateral and one quarter bilateral.

147 patients with recent or old *ecf* (113 boys, 34 girls with a total of 179 hips as the condition was bilateral in 32 patients) which were treated in the *Orthopaedic Hospital, Aarhus* (OHA) during the period 1936—49 were followed-up. The longest period of observation was 42 years, the shortest 3—4 years while the majority were followed-up after approximately 10 years.

RADIOLOGICAL FINDINGS

In 32 of the 147 cases treated in OHA the condition had not been recognized (21.8 per cent.). 22 had undergone X-ray examination but the pictures were either misdiagnosed (11 cases) and classified as Calvé-Legg-Perthe's disease, coxitis or the sequelae of rickets or they were interpreted as normal (11 cases). On follow-up examination, 179 hips could be divided into 5 radiological types on the basis of characteristic changes in the configuration of the head and neck of the femur. A great majority of the patients showed pronounced hip changes.

ETIOLOGY

Familial incidence was encountered in 7 patients (4.8 per cent.). Overloading, trauma and hard work aggravated the disease but were scarcely the original cause as nearly all patients had previously had symptoms for at shorter or longer period. Dyshormonal types (dystrophia adiposogenitalis, infantilism) was more frequent (20.4 per cent.) than in a normal material (5—6 per cent.) but the dyshormonal features disappeared in the course of a few years. Hormone analyses supplied no criteria for dyshormonal etiology. The etiology thus remains obscure.

TREATMENT

Of 179 hips, 120 were treated prior to epiphyseal fusion and in immediate connection with the recognition of the disease, while 37 were treated late and 22 were never treated. Out of the 120, 35 per cent. were treated conservatively (rest in bed, hip spica, Thomas' splint, extension) and 45 per cent. were treated operatively (inforation, nailing, osteotomy). 20 per cent. were treated with bloodless reposition + hip spica or extension.

RESULTS OF TREATMENT

The functional results are evaluated according to a schema which includes subjective symptoms from the hip, shortening of the extremity, soft-tissue atrophy, limp, index of mobility (Gade-Jerre's method) and capacity for work. The results are classified as good, fair and poor.

After treatment of the 120 hips which were treated prior to epiphyseal fusion, it became obvious that the conservative methods and bloodless reposition were less effective in fixing the head than were the operative methods employed. In addition, bloodless reposition of the head was successfull in a few cases only. In untreated hips, the displacement of the head was pronounced in the majority of cases.

Conservative treatment of *slight ecf* rendered good results (50 per cent.) but many were only fair or poor. In a great majority (88 per cent.), operative treatment resulted in good function and in no case in poor function. Operative treatment (inforation, nailing in situ) should, therefore, be preferred to conservative treatment in slight *ecf*.

Conservative treatment of *pronounced ecf* rendered poor results (85 per cent.) and the operative methods employed (inforation, osteotomy) proved not much better (57 per cent.). Bloodless reposition rendered many poor and fair results (65 per cent.). Conservative treatment should, therefore not be employed in pronounced *ecf* and bloodless reposition only in particularly suitable cases of acute complete *ecf* with symptoms of short duration. Whether operative reposition is to be preferred in these cases cannot be concluded from the present material.

A comparison between the function and the period of observation shows that hips with slight *ecf* and epiphyseal fusion, in the majority of cases, maintain good function throughout many years and that hips with pronounced *ecf* and epiphyseal fusion result in only fair or poor function in the majority of cases.

The results of treatment in general hospitals, where conservative methods and bloodless reposition were preferred to operative methods, were inferior to those obtained in specialized departments where operative methods predominated. It should therefore be stressed that patients with recent *ecf* should be referred for treatment to specialized departments, as immediate active treatment, carried out by surgeons experienced in the treatment of this disease, is decisive for the functional prognosis. The results also emphasize the fact that conservative methods and bloodless reposition should be replaced by operative methods in cases of recent *ecf*.

37 hips were not treated until after epiphyseal fusion had occurred and 22 hips were never treated. On follow-up examination it appeared that patients with slight *ecf* preserve good function throughout several years despite late treatment or no treatment at all. Poor function and arthrosis, on the other hand, threaten patients with pronounced *ecf* when untreated or treated late.

The risks of necrosis of the head and arthrosis are greater following conservative treatment and bloodless reposition than following the operative methods employed. The functional results are so poor when followed-up over a prolonged period that conservative treatment and bloodless reposition should be abandoned. Necrosis of the head and arthrosis are far more frequent following pronounced than following slight *ecf*.

SOCIAL PROGNOSIS

The social prognosis was favourable in the majority of the cases. Slight *ecf* and preserved joint allowed the majority of the patients to continue in their previous occupations and nearly all were completely fit for work. The sequelae of pronounced *ecf* and destruction of the joint were the most common causes necessitating change of occupation, but despite deformity of the hip, arthrosis and pain, the capacity for work was, however, good in suitable new occupations in the majority of patients. The patients who had to change their occupation were first and foremost those with hard work (employed in agriculture). The majority changed to skilled work in which the capacity for work was maintained in by far the larger number of cases; a lesser number changed to unskilled work which implied reduced capacity for work or incapacity in several cases. Change of occupation to unskilled work must, therefore, be regarded as disadvantageous and should be strongly advised against.

To place the patient in suitable skilled work if this be possible, with regard to his or her abilities, is the best assurance that the patient will not be overloaded. When change of occupation is indicated on account of the defect of the hip and it is possible to place the patient in skilled apprenticeship in light, standing-sitting occupation, social indications for economic help to the patient in this apprenticeship are present. These principles are followed in Denmark.

Address: Amtssygehuset, Aarhus.

Reference:

Oram, V.: Epifyseolysis capitis femoris. Universitetsforlaget i Aarhus 1952.

INVESTIGATIONS ON SHORT TONES WITH SPECIAL REFERENCE TO THE ADAPTATION OF THE HUMAN EAR

SUMMARY OF THESIS

By OLE BENTZEN

The Thesis comprises two main divisions:

I. *Short Tones:*

To produce sound impulses of short duration, a photo-electric contact was constructed, interposed between a tone generator and a loudspeaker. By means of a rotating shutter, the light impulses to the photo-electric cells may be varied in form and duration and produce corresponding variations in the sound impulses. Simultaneously, the contact can guide three mutually independent channels and is equally suitable for the investigation of pure tones and of noise, dependent on the tone and/or noise generators connected.

The significance of the time factor for the acoustic perception was examined in musical individuals who were subjected to sound impulses of a duration of from 5 to 1,000 msec. The tone-pitch and click-pitch thresholds as well as their dependence upon the intensity were examined and on the basis of the experience gained, compared with previous investigations, a definition of a short tone is established. A short tone is defined as a tone of 1/5 to 1/50 second's duration. Within this interval, the time factor constitutes the third dimension of the tone, a dimension which must be known if the tone is to be completely characterized. *The qualitative alteration* in relation to the duration of the tone may be summed up thus:

Duration below 20 msec.:

Pitch depends on duration: Increasing duration changes pitch from zero — to audible — to maximum pitch. The length of the duration at these stages depends on the frequency, intensity and form of the sound impulse. The duration required is least for high frequency, great intensity and gradual onset of the stimulation.

Duration above 20 msec.:

Pitch is independent of duration.

The quantitative alteration may be summed up thus:

Duration below 20 msec.:

Intensity decreases steeply with decreasing duration.

Duration between 20 and 200 msec.:

Intensity is a linear function of the logarithm of the duration.

Duration above 200 msec.:

Intensity is independent of duration.

II. *Adaptation:*

Adrian defines adaptation as a decline in excitability caused by the stimulus apart from the existence of activity. Fatigue means a decline in activity caused by the previous activity of the organ.

A review of the literature concerning animal experiments on the end organs in tactile, visual, olfactory and auditory senses, shows that adaptation is a frequently occurring phenomenon, differing from fatigue in being independent of oxygen pressure in its development and extent.

In experiments registering the action potentials in isolated acoustic nerve fibres in anaesthetized cats, Galambos & Davis showed a reduction in sensitivity during the acoustic stimulation and of the stimulation. In the present experiments, this condition is employed, as the after-effect of adaptation is investigated by short test tones applied in immediate relation to the cessation of the stimulation. From the displacement of the threshold for the test tones, the after-effect,

magnitude and duration were examined in monaural experiments on normal subjects.

After-effect measured for the frequency of the stimulating tone shows that the after-effect increases with the intensity of the stimulus but is independent of the duration and frequency of the stimulus. The recovery-time increases with the intensity and duration of the stimulus up to 1,000 msec.

After-effect measured for frequencies other than that of the stimulating tone shows that the after-effect is greatest at the stimulated frequency, less with higher and least with lower frequencies. With increase of the intensity, the same distribution was encountered but the number of frequencies affected was increased.

The phenomenon of adaptation is never accompanied by tinnitus, etc., and binaural experiments verify that adaptation is of peripheral origin and is due to changes in the organ of Corti.

A differentiation between adaptation and fatigue is very desirable, and on a basis of the literature and the author's own experiments, the following conditions are established which render possible a differentiation of the two phenomena:

1. An after-effect which is (a) shorter than or equal to the stimulus duration, (b) greatest at the stimulated frequency, (c) of the same order of magnitude within the frequency range from 125 to 8,000 cps. and (d) unaccompanied by tinnitus, etc., must be regarded as being due to adaptation.

2. An after-effect which is (a) longer than the stimulus duration, (b) greatest within the range from ½ to 1 octave above the stimulated frequency, (c) of the greatest magnitude from 2,000 to 4,000 cps. and (d) accompanied by tinnitus, etc., must be due to fatigue.

Finally, it is pointed out that adaptation depends predominantly on the intensity of the stimulus, i. e. the component which affects the auditory perceptive organ from the very onset of the stimulus, whereas fatigue depends predominantly on the stimulus duration.

As a result of the adaptation experiments, the introduction of adaptation tests in clinical audiology is proposed (as suggested by Gardner in 1947) in order to render possible the estimation of the nervous capacity of the organ of Corti.

Address: Statens Høreccentral, Kommunehospitalet, Aarhus.

Reference:

Bentzen, Ole: Investigations on Short Tones with Special Reference to the Adaptation of the Human Ear. Universitetsforlaget i Århus 1953.

THE TOXIC EFFECT OF STREPTOMYCIN IN PREGNANCY

The problem whether a certain drug is able to pass the placental barrier between the mother and the foetus is of interest from several points of view. The relation between chemical structure, molecular size, etc., and the ability to pass the membrane is an interesting physiological question. The possibility of using the drug in the treatment of intrauterine infections is another question, and the possible risks to the foetus of administering the drug for therapeutic purposes to the mother is a third one, and not the least important. Nevertheless, this last question has been much neglected in the pharmacological trial of many of the modern potent drugs. It is therefore noteworthy that a group of Danish investigators have found experimental evidence of a special toxic effect of streptomycin in pregnancy. died from haemorrhage during delivery.

In their studies of the toxic effect of streptomycin upon the eighth cranial nerve Riskær, Christensen & Hertz made investigations on the toxic effects of streptomycin and dihydrostreptomycin on pregnant guinea pigs. In none of the living offspring an adverse effect on the vestibular apparatus could be demonstrated, but both drugs led to abortion in a large percentage of the animals. All animals given daily doses over 100 mg. per. kg. aborted within one week. Doses of 10 mg. per kg. caused no abortion, despite 24 days of treatment. Of the animals given 25 and 50 mg. some aborted, while others carried through the pregnancy, but some foeti were stillborn, and one of the pregnant animals died from haemorrhage during delivery.

The foeti surviving intrauterine treatment with streptomycin and dihydrostreptomycin were normal of appearance and had normal functions, especially with regard to vestibular function and hearing. The central nervous system was found to be normal on histological examination. The concentration of antibiotics in the foetal blood was only 2—8 % of the maternal blood concentration.

Placentae from the treaed animals showed marked hyperaemia, haemorrhage, and beginning endometrial necrobiosis already 24 hours after a single dose of 100 mg. per kg. and the changes became excessive after longer treatment.

In clinical experience streptomycin in the usual dosage is well tolerated by pregnant patients. Two cases of abortion during streptomycin treatment for tuberculosis have been reported, but both mothers were in such poor condition that the effect of the treatment upon the pregnancy cannot be assessed. However, the possible toxic effect of the two antibiotics on the placenta should be born in mind. And all drugs which might conceivably be administered to pregnant patients should be thoroughly investigated with regard to a possible toxic effect upon the product of conception.

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F. F.